Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:ssspta1201txs

PASSWORD:
TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * * *

NEWS	1		Web Page URLs for STN Seminar Schedule - N. America
NEWS	2		"Ask CAS" for self-help around the clock
NEWS	3	FEB 25	CA/CAPLUS - Russian Agency for Patents and Trademarks (ROSPATENT) added to list of core patent offices covered
NEWS	4	FEB 28	PATDPAFULL - New display fields provide for legal status data from INPADOC
NEWS	5	FEB 28	BABS - Current-awareness alerts (SDIs) available
NEWS	6	FEB 28	MEDLINE/LMEDLINE reloaded
NEWS	7	MAR 02	GBFULL: New full-text patent database on STN
NEWS	8	MAR 03	REGISTRY/ZREGISTRY - Sequence annotations enhanced
NEWS	9	MAR 03	MEDLINE file segment of TOXCENTER reloaded
NEWS	10	MAR 22	KOREAPAT now updated monthly; patent information enhanced
NEWS	11	MAR 22	Original IDE display format returns to REGISTRY/ZREGISTRY
NEWS	12	MAR 22	PATDPASPC - New patent database available
NEWS	13	MAR 22	REGISTRY/ZREGISTRY enhanced with experimental property tags
NEWS	14	APR 04	EPFULL enhanced with additional patent information and new fields
NEWS	15	APR 04	EMBASE - Database reloaded and enhanced
NEWS	16	APR 18	New CAS Information Use Policies available online
NEWS	17	APR 25	Patent searching, including current-awareness alerts (SDIs), based on application date in CA/CAplus and USPATFULL/USPAT2 may be affected by a change in filing date for U.S. applications.
NEWS	18	APR 28	Improved searching of U.S. Patent Classifications for U.S. patent records in CA/CAplus
NEWS	19	MAY 23	GBFULL enhanced with patent drawing images
NEWS	20	MAY 23	REGISTRY has been enhanced with source information from CHEMCATS
NEWS	21	MAY 26	STN User Update to be held June 6 and June 7 at the SLA 2005 Annual Conference

NEWS EXPRESS	JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005
NEWS HOURS	STN Operating Hours Plus Help Desk Availability
NEWS INTER	General Internet Information
NEWS LOGIN	Welcome Banner and News Items
NEWS PHONE	Direct Dial and Telecommunication Network Access to STN
NEWS WWW	CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 09:59:54 ON 06 JUN 2005

=> file reg

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.21	0.21

FILE 'REGISTRY' ENTERED AT 10:00:05 ON 06 JUN 2005
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 5 JUN 2005 HIGHEST RN 851662-51-6
DICTIONARY FILE UPDATES: 5 JUN 2005 HIGHEST RN 851662-51-6

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

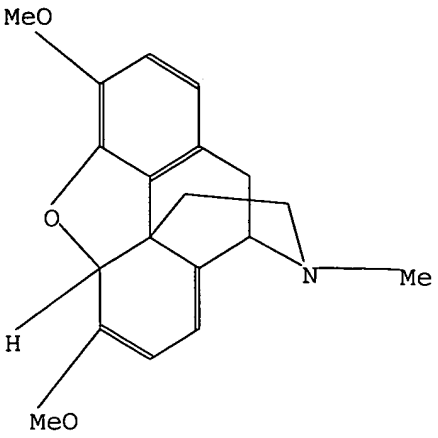
Please note that search-term pricing does apply when conducting SmartSELECT searches.

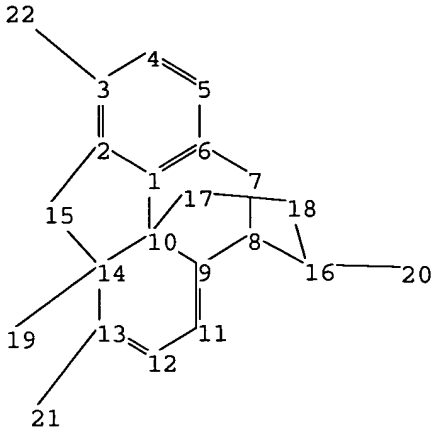
****
*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
*
****

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at:
http://www.cas.org/ONLINE/DBSS/registryss.html

=>
Uploading C:\Program Files\Stnexp\Queries\10722054.str





chain nodes :
19 20 21 22
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
chain bonds :
3-22 13-21 14-19 16-20
ring bonds :
1-2 1-6 1-10 2-3 2-15 3-4 4-5 5-6 6-7 7-8 8-9 8-16 9-10 9-11 10-14
10-17 11-12 12-13 13-14 14-15 16-18 17-18
exact/norm bonds :
1-10 6-7 7-8 8-9 8-16 9-10 9-11 10-14 10-17 11-12 12-13 13-14 16-18
17-18
exact bonds :
2-15 3-22 13-21 14-15 14-19 16-20
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6
isolated ring systems :
containing 1 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:CLASS
20:CLASS 21:CLASS 22:CLASS

L1 STRUCTURE UPLOADED

=> s l1
SAMPLE SEARCH INITIATED 10:00:35 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 125 TO ITERATE

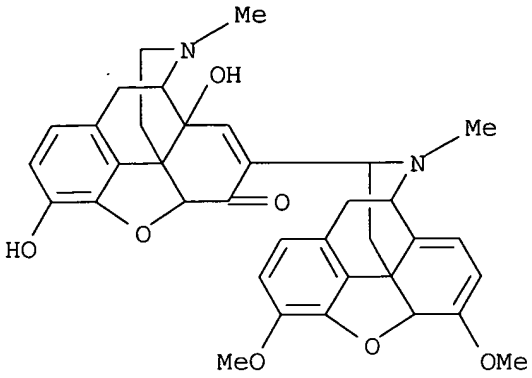
100.0% PROCESSED 125 ITERATIONS 5 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 1830 TO 3170
PROJECTED ANSWERS: 5 TO 234

L2 5 SEA SSS SAM L1

=> d scan

L2 5 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
IN [7,16'-Bimorphinan]-6-one, 6',7,7',8,8',14'-hexadehydro-4,5:4',5'-diepoxy-3,14-dihydroxy-3',6'-dimethoxy-17,17'-dimethyl-, (5α)-(5'α,16'S)- (9CI)
MF C36 H36 N2 O7

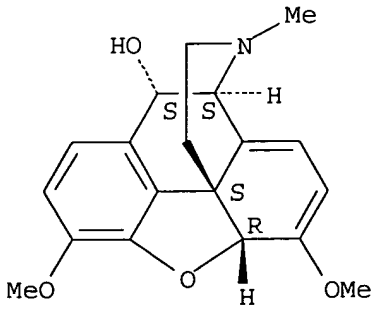


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):4

L2 5 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
IN Morphinan-10-ol, 6,7,8,14-tetradehydro-4,5-epoxy-3,6-dimethoxy-17-methyl-, (5α,10α)- (9CI)
MF C19 H21 N O4

Absolute stereochemistry.



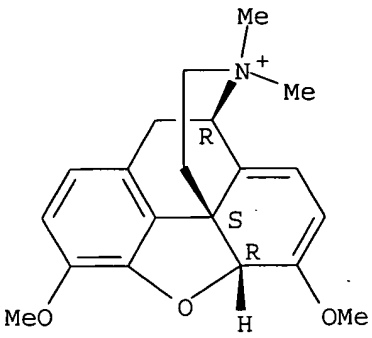
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 5 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
IN Morphinanium, 6,7,8,14-tetradehydro-4,5α-epoxy-3,6-dimethoxy-17,17-dimethyl-, trifluoroacetate (8CI)

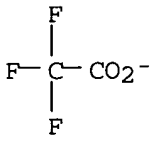
MF C20 H24 N O3 . C2 F3 O2

CM 1

Absolute stereochemistry. Rotation (+).

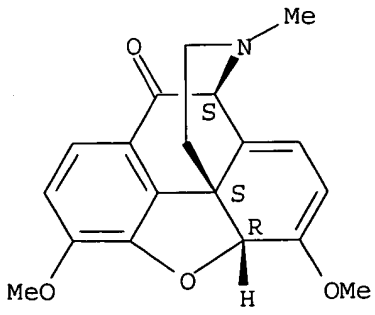


CM 2



L2 5 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
IN Morphinan-10-one, 6,7,8,14-tetradehydro-4,5-epoxy-3,6-dimethoxy-17-methyl-, (5α)- (9CI)
MF C19 H19 N O4

Absolute stereochemistry.



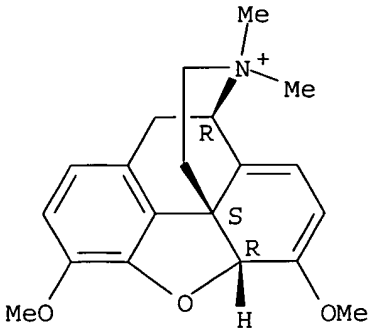
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

L2 5 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
IN Morphinanium, 6,7,8,14-tetradehydro-4,5α-epoxy-3,6-dimethoxy-17,17-dimethyl-, methyl sulfate (8CI)

MF C20 H24 N O3 . C H3 O4 S

CM 1

Absolute stereochemistry. Rotation (+).

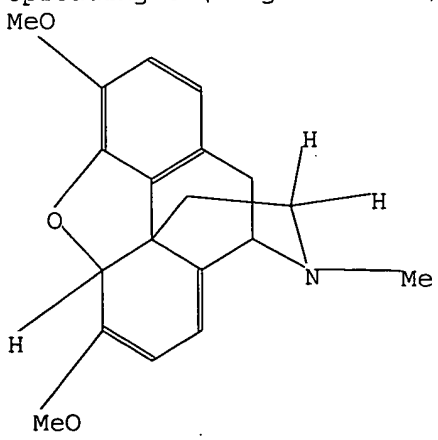


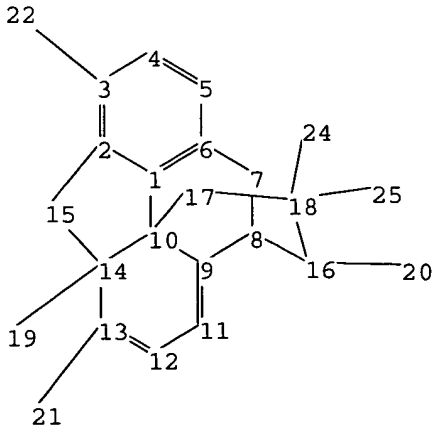
CM 2

Me—O—SO_3^-

ALL ANSWERS HAVE BEEN SCANNED

=>
Uploading C:\Program Files\Stnexp\Queries\107220541.str





chain nodes :
19 20 21 22 24 25
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18
chain bonds :
3-22 13-21 14-19 16-20 18-24 18-25
ring bonds :
1-2 1-6 1-10 2-3 2-15 3-4 4-5 5-6 6-7 7-8 8-9 8-16 9-10 9-11 10-14
10-17 11-12 12-13 13-14 14-15 16-18 17-18
exact/norm bonds :

1-10 6-7 7-8 8-9 8-16 9-10 9-11 10-14 10-17 11-12 12-13 13-14 16-18
17-18
exact bonds :
2-15 3-22 13-21 14-15 14-19 16-20 18-24 18-25
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6
isolated ring systems :
containing 1 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:CLASS
20:CLASS 21:CLASS 22:CLASS 24:CLASS 25:CLASS

L3 STRUCTURE UPLOADED

=> s l3
SAMPLE SEARCH INITIATED 10:03:11 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 125 TO ITERATE

100.0% PROCESSED 125 ITERATIONS 4 ANSWERS
SEARCH TIME: 00.00.01

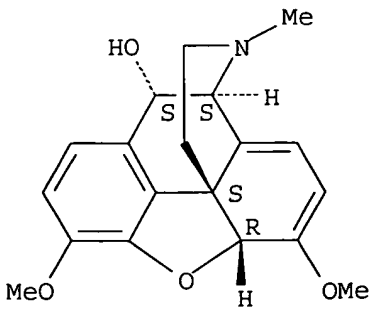
FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 1830 TO 3170
PROJECTED ANSWERS: 4 TO 200

L4 4 SEA SSS SAM L3

=> d scan

L4 4 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
IN Morphinan-10-ol, 6,7,8,14-tetradehydro-4,5-epoxy-3,6-dimethoxy-17-methyl-, (5α,10α)- (9CI)
MF C19 H21 N O4

Absolute stereochemistry.



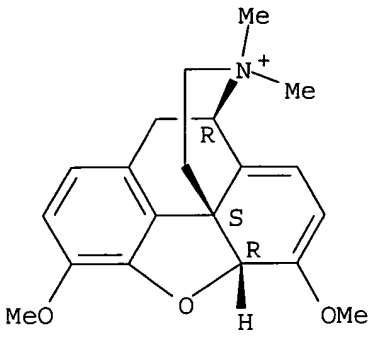
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):3

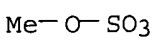
L4 4 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
IN Morphinanium, 6,7,8,14-tetradehydro-4,5α-epoxy-3,6-dimethoxy-17,17-dimethyl-, methyl sulfate (8CI)
MF C20 H24 N O3 . C H3 O4 S

CM 1

Absolute stereochemistry. Rotation (+).



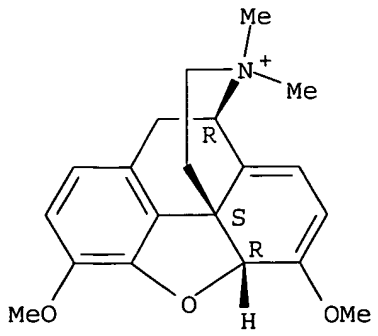
CM 2



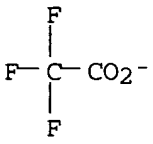
L4 4 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
IN Morphinanium, 6,7,8,14-tetradehydro-4,5α-epoxy-3,6-dimethoxy-17,17-dimethyl-, trifluoroacetate (8CI)
MF C20 H24 N O3 . C2 F3 O2

CM 1

Absolute stereochemistry. Rotation (+).

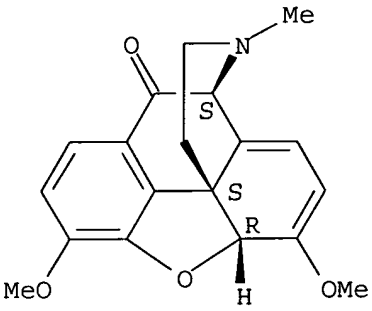


CM 2



L4 4 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
IN Morphinan-10-one, 6,7,8,14-tetradehydro-4,5-epoxy-3,6-dimethoxy-17-methyl-, (5α)- (9CI)
MF C19 H19 N O4

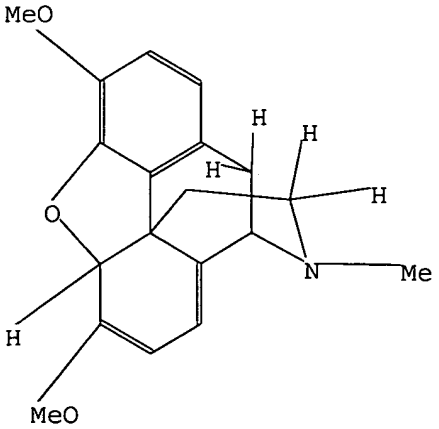
Absolute stereochemistry.

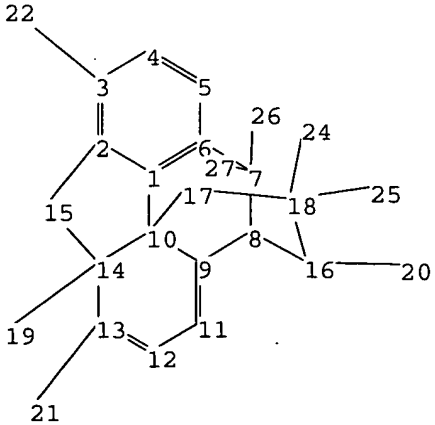


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

ALL ANSWERS HAVE BEEN SCANNED

=>
Uploading C:\Program Files\Stnexp\Queries\107220542.str





chain nodes :
19 20 21 22 24 25 26 27
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18

chain bonds :
3-22 7-26 7-27 13-21 14-19 16-20 18-24 18-25
ring bonds :
1-2 1-6 1-10 2-3 2-15 3-4 4-5 5-6 6-7 7-8 8-9 8-16 9-10 9-11 10-14
10-17 11-12 12-13 13-14 14-15 16-18 17-18
exact/norm bonds :
1-10 6-7 7-8 8-9 8-16 9-10 9-11 10-14 10-17 11-12 12-13 13-14 16-18
17-18
exact bonds :
2-15 3-22 7-26 7-27 13-21 14-15 14-19 16-20 18-24 18-25
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6
isolated ring systems :
containing 1 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:CLASS
20:CLASS 21:CLASS 22:CLASS 24:CLASS 25:CLASS 26:CLASS 27:CLASS

L5 STRUCTURE UPLOADED

=> s l5
SAMPLE SEARCH INITIATED 10:05:14 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 125 TO ITERATE

100.0% PROCESSED 125 ITERATIONS 2 ANSWERS
SEARCH TIME: 00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
BATCH **COMPLETE**
PROJECTED ITERATIONS: 1830 TO 3170
PROJECTED ANSWERS: 2 TO 124

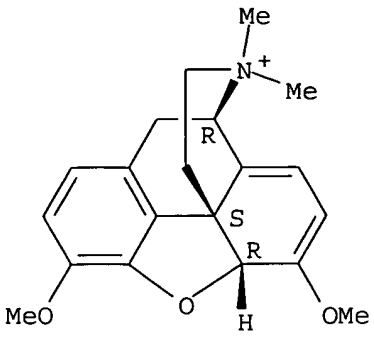
L6 2 SEA SSS SAM L5

=> d scan

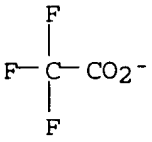
L6 2 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
IN Morphinanium, 6,7,8,14-tetradehydro-4,5α-epoxy-3,6-dimethoxy-17,17-dimethyl-, trifluoroacetate (8CI)
MF C20 H24 N O3 . C2 F3 O2

CM 1

Absolute stereochemistry. Rotation (+).



CM 2

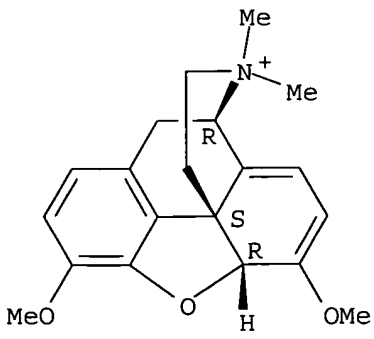


HOW MANY MORE ANSWERS DO YOU WISH TO SCAN? (1):1

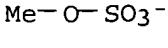
L6 2 ANSWERS REGISTRY COPYRIGHT 2005 ACS on STN
IN Morphinanium, 6,7,8,14-tetradehydro-4,5α-epoxy-3,6-dimethoxy-17,17-dimethyl-, methyl sulfate (8CI)
MF C20 H24 N O3 . C H3 O4 S

CM 1

Absolute stereochemistry. Rotation (+).



CM 2



ALL ANSWERS HAVE BEEN SCANNED

```
=> s l5 ful
FULL SEARCH INITIATED 10:05:39 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED -   2564 TO ITERATE

100.0% PROCESSED    2564 ITERATIONS                                  66 ANSWERS
SEARCH TIME: 00.00.01

L7            66 SEA SSS FUL L5

=> s l7 and (prepar? or method or make or made or synthes? or process)
            212 PREPAR?
              5 METHOD
              5 MAKE
             18 MADE
           1483 SYNTHES?
             62 PROCESS
             11 PROCESSES
             73 PROCESS
                (PROCESS OR PROCESSES)
L8            0 L7 AND (PREPAR? OR METHOD OR MAKE OR MADE OR SYNTHES? OR PROCESS
                )

=> s l7 and (thebaine or N-methylmorphinan)
           1360 THEBAINE
        6055035 N
           1596 METHYLMORPHINAN
            115 N-METHYLMORPHINAN
                (N(W)METHYLMORPHINAN)
L9           30 L7 AND (THEBAINE OR N-METHYLMORPHINAN)

=> d l9 ibib hitstr abs 1-30
'IBIB' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'
'HITSTR' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'
'ABS' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'

The following are valid formats:

Substance information can be displayed by requesting individual
fields or predefined formats.  The predefined substance formats
are:  (RN = CAS Registry Number)

REG     - RN
SAM     - Index Name, MF, and structure - no RN
FIDE    - All substance data, except sequence data
IDE     - FIDE, but only 50 names
SQIDE   - IDE, plus sequence data
SQIDE3  - Same as SQIDE, but 3-letter amino acid codes are used
SQD     - Protein sequence data, includes RN
SQD3    - Same as SQD, but 3-letter amino acid codes are used
SQN     - Protein sequence name information, includes RN

CALC    - Table of calculated properties
EPROP   - Table of experimental properties
PROP    - EPROP and CALC
```

Any CA File format may be combined with any substance format to obtain CA references citing the substance. The substance formats must be cited first. The CA File predefined formats are:

ABS -- Abstract
APPS -- Application and Priority Information
BIB -- CA Accession Number, plus Bibliographic Data
CAN -- CA Accession Number
CBIB -- CA Accession Number, plus Bibliographic Data (compressed)
IND -- Index Data
IPC -- International Patent Classification
PATS -- PI, SO
STD -- BIB, IPC, and NCL

IABS -- ABS, indented, with text labels
IBIB -- BIB, indented, with text labels
ISTD -- STD format, indented

OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

The ALL format gives FIDE BIB ABS IND RE, plus sequence data when it is available.
The MAX format is the same as ALL.
The IALL format is the same as ALL with BIB ABS and IND indented, with text labels.

For additional information, please consult the following help messages:

HELP DFIELDS -- To see a complete list of individual display fields.
HELP FORMATS -- To see detailed descriptions of the predefined formats.
ENTER DISPLAY FORMAT (IDE):end

=> d hits
'HITS' IS NOT A VALID FORMAT FOR FILE 'REGISTRY'

The following are valid formats:

Substance information can be displayed by requesting individual fields or predefined formats. The predefined substance formats are: (RN = CAS Registry Number)

REG - RN
SAM - Index Name, MF, and structure - no RN
FIDE - All substance data, except sequence data
IDE - FIDE, but only 50 names
SQIDE - IDE, plus sequence data
SQIDE3 - Same as SQIDE, but 3-letter amino acid codes are used
SQD - Protein sequence data, includes RN
SQD3 - Same as SQD, but 3-letter amino acid codes are used
SQN - Protein sequence name information, includes RN

CALC - Table of calculated properties
EPROP - Table of experimental properties
PROP - EPROP and CALC

Any CA File format may be combined with any substance format to obtain CA references citing the substance. The substance formats must be cited first. The CA File predefined formats are:

ABS -- Abstract
APPS -- Application and Priority Information
BIB -- CA Accession Number, plus Bibliographic Data
CAN -- CA Accession Number
CBIB -- CA Accession Number, plus Bibliographic Data (compressed)
IND -- Index Data
IPC -- International Patent Classification
PATS -- PI, SO
STD -- BIB, IPC, and NCL

IABS -- ABS, indented, with text labels
IBIB -- BIB, indented, with text labels
ISTD -- STD format, indented

OBIB -------- AN, plus Bibliographic Data (original)
OIBIB ------- OBIB, indented with text labels

SBIB -------- BIB, no citations
SIBIB ------- IBIB, no citations

The ALL format gives FIDE BIB ABS IND RE, plus sequence data when it is available.
The MAX format is the same as ALL.
The IALL format is the same as ALL with BIB ABS and IND indented, with text labels.

For additional information, please consult the following help messages:

HELP DFIELDS -- To see a complete list of individual display fields.
HELP FORMATS -- To see detailed descriptions of the predefined formats.
ENTER DISPLAY FORMAT (IDE):end

=> d hist

(FILE 'HOME' ENTERED AT 09:59:54 ON 06 JUN 2005)

FILE 'REGISTRY' ENTERED AT 10:00:05 ON 06 JUN 2005
L1 STRUCTURE UPLOADED
L2 5 S L1
L3 STRUCTURE UPLOADED
L4 4 S L3
L5 STRUCTURE UPLOADED
L6 2 S L5
L7 66 S L5 FUL
L8 0 S L7 AND (PREPAR? OR METHOD OR MAKE OR MADE OR SYNTHES? OR PROC
L9 30 S L7 AND (THEBAINE OR N-METHYLMORPHINAN)

=> file caplus

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	210.90	211.11

FILE 'CAPLUS' ENTERED AT 10:11:53 ON 06 JUN 2005

FILE COVERS 1907 - 6 Jun 2005 VOL 142 ISS 24
FILE LAST UPDATED: 5 Jun 2005 (20050605/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> s l7 and (prepar? or method or make or made or synthes? or process)
          1409 L7
       1550981 PREPAR?
        116278 PREP
          2042 PREPS
        118120 PREP
                 (PREP OR PREPS)
       1933532 PREPD
            21 PREPDS
       1933547 PREPD
                 (PREPD OR PREPDS)
        108210 PREPG
            12 PREPGS
        108221 PREPG
                 (PREPG OR PREPGS)
       2579035 PREPN
        199665 PREPNS
       2730261 PREPN
                 (PREPN OR PREPNS)
       4526186 PREPAR?
                 (PREPAR? OR PREP OR PREPD OR PREPG OR PREPN)
       2844689 METHOD
       1184511 METHODS
       3695906 METHOD
                 (METHOD OR METHODS)
        209758 MAKE
        162625 MAKES
        361748 MAKE
                 (MAKE OR MAKES)
       1149491 MADE
            24 MADES
       1149512 MADE
                 (MADE OR MADES)
       1450411 SYNTHES?
       2091578 PROCESS
       1400935 PROCESSES
```

```
       3114301 PROCESS
                 (PROCESS OR PROCESSES)
L10         773 L7 AND (PREPAR? OR METHOD OR MAKE OR MADE OR SYNTHES? OR PROCESS
                )

=> s l9 and (prepar? or method or make or made or synthes? or process)
          1406 L9
       1550981 PREPAR?
        116278 PREP
          2042 PREPS
        118120 PREP
                 (PREP OR PREPS)
       1933532 PREPD
            21 PREPDS
       1933547 PREPD
                 (PREPD OR PREPDS)
        108210 PREPG
            12 PREPGS
        108221 PREPG
                 (PREPG OR PREPGS)
       2579035 PREPN
        199665 PREPNS
       2730261 PREPN
                 (PREPN OR PREPNS)
       4526186 PREPAR?
                 (PREPAR? OR PREP OR PREPD OR PREPG OR PREPN)
       2844689 METHOD
       1184511 METHODS
       3695906 METHOD
                 (METHOD OR METHODS)
        209758 MAKE
        162625 MAKES
        361748 MAKE
                 (MAKE OR MAKES)
       1149491 MADE
            24 MADES
       1149512 MADE
                 (MADE OR MADES)
       1450411 SYNTHES?
       2091578 PROCESS
       1400935 PROCESSES
       3114301 PROCESS
                 (PROCESS OR PROCESSES)
L11         771 L9 AND (PREPAR? OR METHOD OR MAKE OR MADE OR SYNTHES? OR PROCESS
                )

=> dup rem l10 l11
PROCESSING COMPLETED FOR L10
PROCESSING COMPLETED FOR L11
L12          773 DUP REM L10 L11 (771 DUPLICATES REMOVED)

=> s l12 and (8-methoxy-dihydrthebaine or codeinone dimethyl ketal or neopinone
dimethyl ketal or codeinone)
L13         772 S L12
L14           1 S L12
       2591351 8
        135093 METHOXY
             0 DIHYDRTHEBAINE
             0 8-METHOXY-DIHYDRTHEBAINE
```

```
                (8(W)METHOXY(W)DIHYDRTHEBAINE)
           660 CODEINONE
            37 CODEINONES
           671 CODEINONE
                (CODEINONE OR CODEINONES)
        331113 DIMETHYL
            42 DIMETHYLS
        331134 DIMETHYL
                (DIMETHYL OR DIMETHYLS)
          9480 KETAL
          3950 KETALS
         11354 KETAL
                (KETAL OR KETALS)
             3 CODEINONE DIMETHYL KETAL
                (CODEINONE(W)DIMETHYL(W)KETAL)
            45 NEOPINONE
             4 NEOPINONES
            48 NEOPINONE
                (NEOPINONE OR NEOPINONES)
        331113 DIMETHYL
            42 DIMETHYLS
        331134 DIMETHYL
                (DIMETHYL OR DIMETHYLS)
          9480 KETAL
          3950 KETALS
         11354 KETAL
                (KETAL OR KETALS)
             1 NEOPINONE DIMETHYL KETAL
                (NEOPINONE(W)DIMETHYL(W)KETAL)
           660 CODEINONE
            37 CODEINONES
           671 CODEINONE
                (CODEINONE OR CODEINONES)
L15          90 (L13 OR L14) AND (8-METHOXY-DIHYDRTHEBAINE OR CODEINONE DIMETHYL
                KETAL OR NEOPINONE DIMETHYL KETAL OR CODEINONE)

=> s l12 and (8-methoxy-dihydrothebaine or codeinone dimethyl ketal or neopinone
dimethyl ketal or codeinone)
L16         772 S L12
L17           1 S L12
       2591351 8
        135093 METHOXY
            82 DIHYDROTHEBAINE
             1 DIHYDROTHEBAINES
            82 DIHYDROTHEBAINE
                (DIHYDROTHEBAINE OR DIHYDROTHEBAINES)
             0 8-METHOXY-DIHYDROTHEBAINE
                (8(W)METHOXY(W)DIHYDROTHEBAINE)
           660 CODEINONE
            37 CODEINONES
           671 CODEINONE
                (CODEINONE OR CODEINONES)
        331113 DIMETHYL
            42 DIMETHYLS
        331134 DIMETHYL
                (DIMETHYL OR DIMETHYLS)
          9480 KETAL
          3950 KETALS
         11354 KETAL
```

```
                (KETAL OR KETALS)
             3  CODEINONE DIMETHYL KETAL
                (CODEINONE(W)DIMETHYL(W)KETAL)
            45  NEOPINONE
             4  NEOPINONES
            48  NEOPINONE
                (NEOPINONE OR NEOPINONES)
        331113  DIMETHYL
            42  DIMETHYLS
        331134  DIMETHYL
                (DIMETHYL OR DIMETHYLS)
          9480  KETAL
          3950  KETALS
         11354  KETAL
                (KETAL OR KETALS)
             1  NEOPINONE DIMETHYL KETAL
                (NEOPINONE(W)DIMETHYL(W)KETAL)
           660  CODEINONE
            37  CODEINONES
           671  CODEINONE
                (CODEINONE OR CODEINONES)
L18         90  (L16 OR L17) AND (8-METHOXY-DIHYDROTHEBAINE OR CODEINONE DIMETHY
                L KETAL OR NEOPINONE DIMETHYL KETAL OR CODEINONE)

=> s l12 and (8-methoxy-delta-dihydrothebaine or codeinone dimethyl ketal or
neopinone dimethyl ketal or codeinone)
L19        772  S L12
L20          1  S L12
       2591351  8
        135093  METHOXY
        433030  DELTA
           376  DELTAS
        433211  DELTA
                (DELTA OR DELTAS)
            82  DIHYDROTHEBAINE
             1  DIHYDROTHEBAINES
            82  DIHYDROTHEBAINE
                (DIHYDROTHEBAINE OR DIHYDROTHEBAINES)
             0  8-METHOXY-DELTA-DIHYDROTHEBAINE
                (8(W)METHOXY(W)DELTA(W)DIHYDROTHEBAINE)
           660  CODEINONE
            37  CODEINONES
           671  CODEINONE
                (CODEINONE OR CODEINONES)
        331113  DIMETHYL
            42  DIMETHYLS
        331134  DIMETHYL
                (DIMETHYL OR DIMETHYLS)
          9480  KETAL
          3950  KETALS
         11354  KETAL
                (KETAL OR KETALS)
             3  CODEINONE DIMETHYL KETAL
                (CODEINONE(W)DIMETHYL(W)KETAL)
            45  NEOPINONE
             4  NEOPINONES
            48  NEOPINONE
                (NEOPINONE OR NEOPINONES)
        331113  DIMETHYL
```

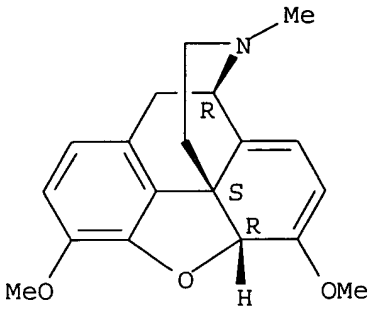
```
            42 DIMETHYLS
        331134 DIMETHYL
                 (DIMETHYL OR DIMETHYLS)
          9480 KETAL
          3950 KETALS
         11354 KETAL
                 (KETAL OR KETALS)
             1 NEOPINONE DIMETHYL KETAL
                 (NEOPINONE(W)DIMETHYL(W)KETAL)
           660 CODEINONE
            37 CODEINONES
           671 CODEINONE
                 (CODEINONE OR CODEINONES)
L21          90 (L19 OR L20) AND (8-METHOXY-DELTA-DIHYDROTHEBAINE OR CODEINONE
               DIMETHYL KETAL OR NEOPINONE DIMETHYL KETAL OR CODEINONE)

=> s l12 and (dihydrothebaine or codeinone dimethyl ketal or neopinone dimethyl
ketal or codeinone)
L22         772 S L12
L23           1 S L12
             82 DIHYDROTHEBAINE
              1 DIHYDROTHEBAINES
             82 DIHYDROTHEBAINE
                 (DIHYDROTHEBAINE OR DIHYDROTHEBAINES)
           660 CODEINONE
            37 CODEINONES
           671 CODEINONE
                 (CODEINONE OR CODEINONES)
        331113 DIMETHYL
            42 DIMETHYLS
        331134 DIMETHYL
                 (DIMETHYL OR DIMETHYLS)
          9480 KETAL
          3950 KETALS
         11354 KETAL
                 (KETAL OR KETALS)
             3 CODEINONE DIMETHYL KETAL
                 (CODEINONE(W)DIMETHYL(W)KETAL)
            45 NEOPINONE
             4 NEOPINONES
            48 NEOPINONE
                 (NEOPINONE OR NEOPINONES)
        331113 DIMETHYL
            42 DIMETHYLS
        331134 DIMETHYL
                 (DIMETHYL OR DIMETHYLS)
          9480 KETAL
          3950 KETALS
         11354 KETAL
                 (KETAL OR KETALS)
             1 NEOPINONE DIMETHYL KETAL
                 (NEOPINONE(W)DIMETHYL(W)KETAL)
           660 CODEINONE
            37 CODEINONES
           671 CODEINONE
                 (CODEINONE OR CODEINONES)
L24         114 (L22 OR L23) AND (DIHYDROTHEBAINE OR CODEINONE DIMETHYL KETAL
               OR NEOPINONE DIMETHYL KETAL OR CODEINONE)
```

```
=> s l24 and acid
       3984993 ACID
       1478122 ACIDS
       4463578 ACID
                 (ACID OR ACIDS)
L25         45 L24 AND ACID

=> s l25 and base
        632361 BASE
        145420 BASES
        721217 BASE
                 (BASE OR BASES)
L26         18 L25 AND BASE

=> d l26 ibib hitstr abs 1-18

L26  ANSWER 1 OF 18  CAPLUS  COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:         2004:1080779  CAPLUS
DOCUMENT NUMBER:          142:38409
TITLE:                    Process for manufacturing oxycodone from
                          codeine
INVENTOR(S):              Lin, Zhaiwei; Francis, Charles Auxilium; Kaldahl,
                          Christopher Arne; Antczak, Kazimierz Grzegorz; Kumar,
                          Vijai
PATENT ASSIGNEE(S):       Halsey Drug Company, USA
SOURCE:                   PCT Int. Appl., 15 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 English
FAMILY ACC. NUM. COUNT:   2
PATENT INFORMATION:

     PATENT NO.           KIND   DATE        APPLICATION NO.          DATE
     --------------       ----   --------    --------------------     --------
     WO 2004108090         A2    20041216    WO 2004-US17891          20040604
     WO 2004108090         A3    20050324
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
             CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
             GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
             LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
             NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
             TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
         RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
             AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
             EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
             SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
             SN, TD, TG
     US 6864370            B1    20050308    US 2003-455202           20030605
PRIORITY APPLN. INFO.:                       US 2003-455202       A   20030605
OTHER SOURCE(S):          CASREACT 142:38409
IT   94713-28-7P, Thebaine bitartrate
     RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
     (Reactant or reagent)
        (preparation and oxidation of, with hydrogen peroxide;
        process for manufacturing oxycodone from codeine)
RN   94713-28-7  CAPLUS
CN   Morphinan, 6,7,8,14-tetradehydro-4,5-epoxy-3,6-dimethoxy-17-methyl-,
     (5α)-, (2R,3R)-2,3-dihydroxybutanedioate (1:1) (9CI)  (CA INDEX
     NAME)
```

CM 1

CRN 115-37-7
CMF C19 H21 N O3

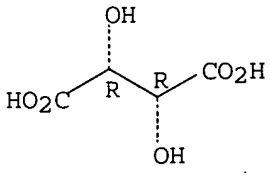
Absolute stereochemistry.



CM 2

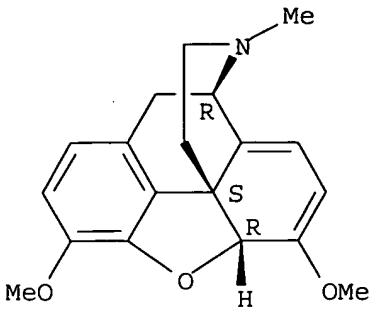
CRN 87-69-4
CMF C4 H6 O6

Absolute stereochemistry.



IT **115-37-7P**, Thebaine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(**preparation** and oxidation of; **process** for manufacturing oxycodone from codeine)
RN 115-37-7 CAPLUS
CN Morphinan, 6,7,8,14-tetradehydro-4,5-epoxy-3,6-dimethoxy-17-methyl-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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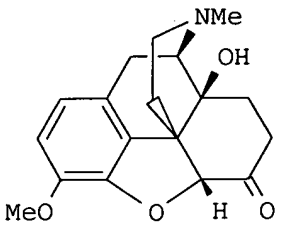

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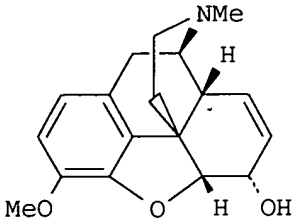


II

AB Oxycodone (I) is manufactured in high yields and with a high purity using codeine (II) or a salt of codeine as the starting material. The manufacturing **process** involves the following steps: (a) codeine or a codeine salt (e.g., codeine phosphate) is converted into the intermediate N-carboalkoxy- or N-carboaryloxynorcodeine; (b) the intermediate N-carboalkoxy- or N-carboaryloxynorcodeine resulting from step (a) is oxidized to yield the intermediate N-carboalkoxy- or N-carboaryloxynorcodeinone; (c) the intermediate N-carboalkoxy- or N-carboaryloxynorcodeinone resulting from step (b) is enolized with a **base** and the resultant enolate is thereafter methylated to yield the intermediate N-carboalkoxy- or N-carboaryloxynorthebaine; (d) the intermediate N-carboalkoxy- or N-carboaryloxynorthebaine resulting from step (c) is reduced to yield thebaine; (e) the thebaine resulting from step (d) is oxidized to yield the intermediate 14-hydroxycodeinone; and (f) the intermediate 14-hydroxycodeinone resulting from step (e) is hydrogenated to yield oxycodone.

L26 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:430807 CAPLUS
DOCUMENT NUMBER: 141:7329
TITLE: **Preparation** of quaternary salts of morphinan alkaloids
INVENTOR(S): Cantrell, Gary L.; Halvachs, Robert E.
PATENT ASSIGNEE(S): Mallinckrodt Inc., USA
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004043964	A2	20040527	WO 2003-US35463	20031105
WO 2004043964	A3	20040826		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

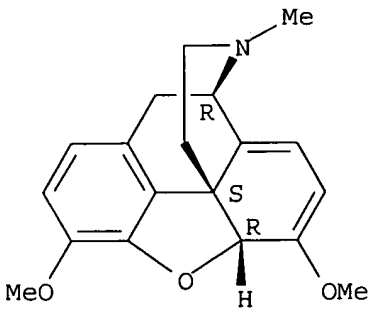
PRIORITY APPLN. INFO.: US 2002-424748P P 20021108
US 2002-425580P P 20021112

OTHER SOURCE(S): CASREACT 141:7329; MARPAT 141:7329

IT **115-37-7**, Thebaine
RL: RCT (Reactant); RACT (Reactant or reagent)
(**preparation** of quaternary salts of morphinan alkaloids from tertiary N-substituted morphinan alkaloid and alkyl halide in an anhydrous solvent system)

RN 115-37-7 CAPLUS
CN Morphinan, 6,7,8,14-tetradehydro-4,5-epoxy-3,6-dimethoxy-17-methyl-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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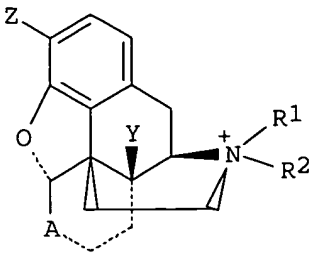

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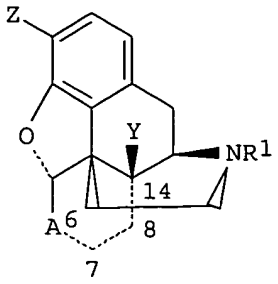
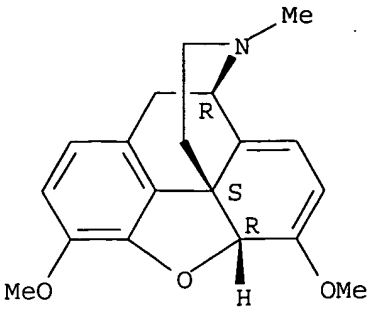


II

AB The present invention discloses a **process** for **preparation** of quaternary salts of morphinan alkaloids, such as I.X- [A = CO, CS, C:CH2, CHA1, CA1:; A1 = OH, alkoxy, acyloxy; R1, R2 = hydrocarbyl; X- = anion; Y, if present = H, OH, alkoxy, acyloxy; Z = OH, alkoxy, acyloxy; dashed lines = single bond; dashed line between 6 and 7 and between 8 and 14 = single bond and between 7 and 8 = double bond; dashed line between 6 and 7 and between 8 and 14 = double bod and between 7 and 8 = single bond], by the reaction of tertiary N-substituted morphinan alkaloid II with an alkyl halide in an anhydrous solvent system, wherein the solvent system comprises an aprotic dipolar solvent with the aprotic dipolar solvent constituting at least 25 wt% of the solvent system. Thus, N-cyclopropylmethyl-noroxymorphone methobromide I [A = CO; dashed line = single bond; Y = H; Z = OH, R1 = CH2CH(CH2)2; R2 = Me] was **prepd** . by the reaction between Me bromide and naltrexone anhydrous **base** II [A = CO; dashed line = single bond; Y = H; Z = OH, R1 = CH2CH(CH2)2] in 1-methyl-2-pyrrolidone.

L26 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1966:507206 CAPLUS
DOCUMENT NUMBER: 65:107206
ORIGINAL REFERENCE NO.: 65:19930b-c
TITLE: Analysis of drugs and chemicals by infrared absorption spectra. VII. Rapid simultaneous determination of acetanilide and phenacetin in pharmaceutical **preparations** containing acetanilide, phenacetin, and caffeine
AUTHOR(S): Oi, Naobumi
CORPORATE SOURCE: Sumitomo Chem. Co., Osaka, Japan
SOURCE: Yakugaku Zasshi (1966), 86(9), 859-60
CODEN: YKKZAJ; ISSN: 0031-6903
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
IT **115-37-7**, Thebaine
(determination of)
RN 115-37-7 CAPLUS
CN Morphinan, 6,7,8,14-tetradehydro-4,5-epoxy-3,6-dimethoxy-17-methyl-, (5α)- (9CI) (CA INDEX NAME)

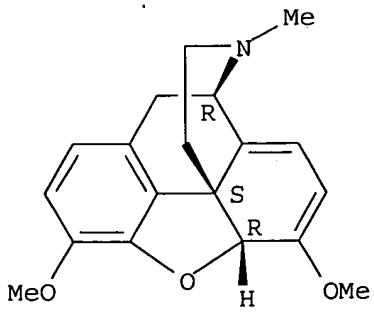
Absolute stereochemistry.



AB cf. CA 64, 4870f. A simple ir spectrometric **method** is offered for rapid determination of acetanilide (I) and phenacetin (II) in pharmaceutical **prepns.** containing I, II, and caffeine. Me2CO is chosen as the solvent, and the key bands used for I and II are 695 and 827 cm.-1, resp. These 2 components can be determined easily without interference of other components by the use of two available **base** lines.

L26 ANSWER 4 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1966:36064 CAPLUS
DOCUMENT NUMBER: 64:36064
ORIGINAL REFERENCE NO.: 64:6701h,6702h,6703a-b
TITLE: Ultraviolet absorption spectra of some pharmaceutical **preparations**, derivatives of isoquinoline
AUTHOR(S): Pinyazhko, I. R. M.
CORPORATE SOURCE: Med. Inst., Lvov
SOURCE: Farmatsevtichnii Zhurnal (Kiev) (1964), 19(6), 12-16
CODEN: FRZKAP; ISSN: 0367-3057
DOCUMENT TYPE: Journal
LANGUAGE: Ukrainian
IT **115-37-7**, Thebaine
(spectrum of)
RN 115-37-7 CAPLUS
CN Morphinan, 6,7,8,14-tetradehydro-4,5-epoxy-3,6-dimethoxy-17-methyl-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

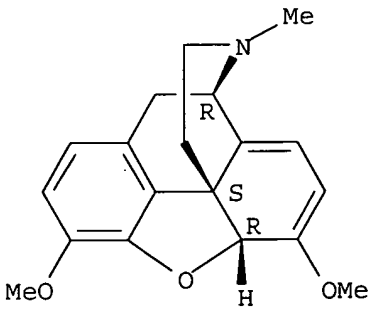


GI For diagram(s), see printed CA Issue.
AB cf. Ca 64, 4871a. The effect of substituents and of mol. structure is studied in the following 19 derivs. of isoquinoline in the uv spectra: papaverine hydrochloride (I), narcotine hydrochloride (II), narceine

hydrochloride (III), apomorphine (IV), salsoline hydrochloride (V), salsolidine **base** (VI), emetine hydrochloride (VII), oxyacanthine (VIII), hydrastine (IX), morphine hydrochloride (X), codeine (XI), codeine phosphate (XII), thebaine (XIII), ethylmorphine hydrochloride (XIV), heroine hydrochloride (XV), hydrocodone phosphate (XVI), tecodine (XVII), hydrastinine hydrochloride (XVIII), and stypticine (XIX). The spectra were taken in concns. of 1-10 mg./100 ml. of 95% EtoH. In the short-wave K band at 230 mμ a bathochromic shift is observed in I: 238 (log ε 4.71), II: 238 (4.44), XVIII: 252 (4.28), XIX: 253 (4.07), and in III, IV, VIII, and X-XVIII the band is <220 mμ. The phenol band is observed at 280-5 mμ in most compds. except III: 270, IX: 297, XVIII: 305. The long-wave band at 300 mμ appears only in I: 315 (3.62), 325 (3.64); II: 310 (3.72); IV: 308 (3.56); XVIII: 367 (3.96); XIX: 334 (4.20). This is due to the hydrated pyridine ring in those mols. Comparison of the spectra of the derivs. and the model mols. (phenol, pyrocatechol, guaiacol, and veratrole) show that in the other 13 hydroisoquinoline derivs. (and III) the chromophore is A and the substituents shift only the maximum batho- or hypsochromically.

L26 ANSWER 5 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1965:82758 CAPLUS
DOCUMENT NUMBER: 62:82758
ORIGINAL REFERENCE NO.: 62:14739b-f
TITLE: A new **method** for the **preparation** of **codeinone** from thebaine
AUTHOR(S): Gavard, Jean Pierre; Krausz, Francois; Rull, Thomas; Delfly, Michel
SOURCE: Bulletin de la Societe Chimique de France (1965), (2), 486-90
CODEN: BSCFAS; ISSN: 0037-8968
DOCUMENT TYPE: Journal
LANGUAGE: French
IT **115-37-7**, Thebaine
(**codeinone preparation** from)
RN 115-37-7 CAPLUS
CN Morphinan, 6,7,8,14-tetradehydro-4,5-epoxy-3,6-dimethoxy-17-methyl-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

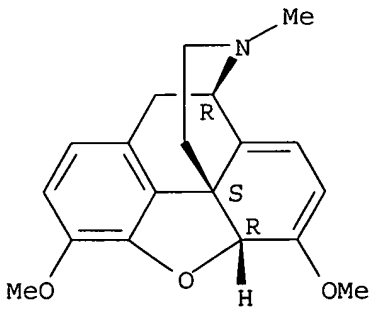


GI For diagram(s), see printed CA Issue.
AB Dry HCl (40 g.) was added to 300 ml. dry iso-Pr2O at -15°. To this was added a solution of 50 g. thebaine (I) in 230 ml. CH2Cl2. The solution was maintained at 10° 3 hrs., then added to a suspension of 94 g. NaHCO3 in 300 ml. H2O, and the pH adjusted to 8. Extraction gave 50% crude **codeinone** (II), m. 185 (EtOAc). Similar treatment of a solution of

124 g. I in 600 ml. CH2Cl2 with a solution of 140 g. HBr in 600 ml. dibutyl ether at 0° gave 76% crude II. A similar reaction using NaOMe as **base** in MeOH gave 8β-bromo-6-methoxy-6,7,8,14-tetrahydrothebaine (IIIa), m. 144° (MeOH-) [α]D -43° ±3°. A solution of 1 g. IIIa in 10 ml. Me2CO was refluxed 2 hrs. with several drops HCl and 2 crystals p-toluenesulfonic **acid** to give 500 mg. II. Heating to reflux 1.5 g. IIIa with 1.5 g. LiAlH4 in tetrahydrofuran gave on decomposition, extraction, and chromatography on alumina 841 mg. 6-methoxy-6,7,8,14-tetrahydrothebaine (IIIb), m. 121° (MeOH), [α]D -153°. Refluxing IIIb in Me2CO with HCl and p-toluenesulfonic **acid** gave dihydrocodeinone (IIIc), m. 194°, [α]D -205° The reaction of I with HBr and addition to a suspension of tert-BuOK gave starting material. To a solution of 5 g. I in CH2Cl2 was added dropwise 1.1 mole Br. Evaporation and treatment with NaOMe gave 14-bromo-6-methoxy-6,14-**dihydrothebaine** (IV), m. 168-70° (MeOH), [α]D -30°. The reaction of I with HBr is believed to proceed through the intermediate V.

L26 ANSWER 6 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1965:73491 CAPLUS
DOCUMENT NUMBER: 62:73491
ORIGINAL REFERENCE NO.: 62:12979f-h,12980a-d
TITLE: Determination of organic **bases** by semimicrotitrimetry using sodium lauryl sulfate. III. Application in pharmaceutical **preparations**
AUTHOR(S): Pellerin, Fernand; Gautier, Jean Albert; Demay, Dominique
CORPORATE SOURCE: Fac. Pharm., Paris
SOURCE: Ann. Pharm. Franc. (1964), 22(8-9), 559-65
DOCUMENT TYPE: Journal
LANGUAGE: French
IT **115-37-7**, Thebaine
(determination of, in pharmaceuticals)
RN 115-37-7 CAPLUS
CN Morphinan, 6,7,8,14-tetradehydro-4,5-epoxy-3,6-dimethoxy-17-methyl-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

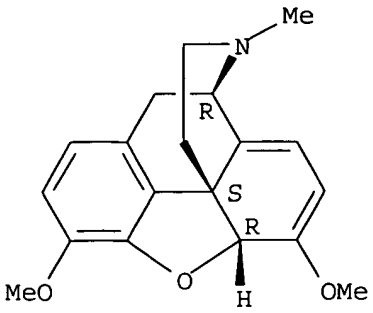


AB The **method** is applied to the determination of 0.01-0.05 millimole each of the following, in the presence of the resp. named compds.: benzethonium chloride (I), 25 mg./100 ml., chloramphenicol, urethan, NaCl, propylene glycol, and H2O; acepromazine maleate (II), 13.5 mg./5 ml.; benzododecinium chloride (III), 50 mg./100 ml., mephetedrine sulfate, chloretone (chlorbutol), extract of bergamot, NaCl, and H2O;

dodecyldimethyl(carbethoxymethyl)ammonium bromide (IV), 1.5 g./100 ml., with pentaethylene glycol dichlorocresol ether and H2O; cethexonium bromide (V), 100 mg./100 ml., EtOH, Me,2CO, NaCl, and H2O; phenoxadrine citrate (VI), sucrose, essential oils, Me p-hydroxybenzoate and yellow **acid** R; propiomazine maleate (VII) in tablets containing VII 45.7, meprobamate 300, Mg stearate 5, and excipients 149.3 mg. (Mg stearate, 5 mg., does not interfere); papaverine (VIII) in tablets containing VIII **base** 10, nicotinic **acid** 10, and excipients 180 mg.; cinnama-verine-HCl (IX) in tablets containing IX and excipients (Levilite 18, Mg stearate 5, talc 18, poly(methylsiloxane) S.I. 200 mg.); dicyclomine-HCl (X) in tablets containing X 10, phenobarbital 15, Ponceau S.X. trace, and excipients 275 mg. To determine X, use 1 ml. of 0.008% Methyl Yellow-0.005% methylene blue indicator (in aqueous 80% EtOH), add 5 ml. 1.8M H2SO4, and titrate with 0.01M Na lauryl sulfate (XI) to the rose color in the aqueous solution, and a violet color in the CHCl3 phase; propanocaine-HCl (XII) is an ointment containing XII 1.5%, eucalyptol, poly(oxyethylene) derivs. (XIII) of fatty alcs., glycerol (XIV), essential oils, and H2O; V in an ointment containing V 0.25%, hydrocortisone, dichlordiphenoxide, XIII, XIV, corn oil (interesterified), lauryl gallate, and V in an ointment containing V 0.25%, cetyl alc., XI 1%, and H2O. To der. V in the presence of XI, dissolve 3-4 g. of the ointment with 10 ml. of 95% EtOH, pass the solution slowly through a 6-8 cm. high column of 6 ml. of Amberlite IRA 400 resin (**prepared** by washing the resin with 2.5M NaOH, H2O, N HCl, and H2O (4 times), and with aqueous 50% EtOH), wash the column with 50% EtOH (three 5-ml. vols. + one 10-ml. volume), evaporate the EtOH from the combined eluate in vacuo; to the aqueous solution, add 10 ml. H2O and 20 ml. CHCl3, and titrate with 0.01M XI as described. The capacity of the resin is 0.35 g. XI/g. Determine promethazine-HCl (XV) in suppositories containing XV 10, aspirin 500 mg., and glycerides (semi-synthetic) 1.49 g., by the described **method** without modifying. The results of the detns. of I-X,XII, and XV are quant. The precision is ±2% of the amount of I-X, XII or XV determined

L26 ANSWER 7 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1965:43253 CAPLUS
DOCUMENT NUMBER: 62:43253
ORIGINAL REFERENCE NO.: 62:7588d
TITLE: **Acid-base** titrations in alcoholic medium. II. The displacement titration of alkaloid salts
AUTHOR(S): Schute, J. B.
CORPORATE SOURCE: Rijksuniv., Leiden, Neth.
SOURCE: Pharmaceutisch Weekblad (1964), 99(39), 1053-70
CODEN: PHWEAW; ISSN: 0031-6911
DOCUMENT TYPE: Journal
LANGUAGE: Dutch
IT **850-57-7**, Thebaine, hydrochloride
(titration of, in nonaq. media)
RN 850-57-7 CAPLUS
CN Morphinan, 6,7,8,14-tetradehydro-4,5-epoxy-3,6-dimethoxy-17-methyl-, hydrochloride, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

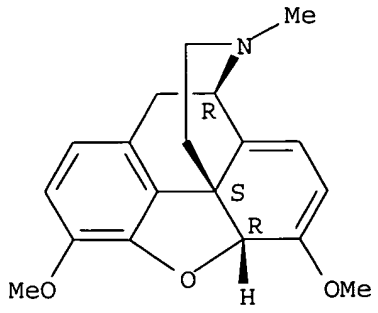


● HCl

AB cf. CA 61, 13856e. A large number of alkaloid salts have been titrated by using the author's **method** (loc. cit.). Solvents used were 96% EtOH, Me2CO-H2O (10:1), and Me2CO-MeOH (4:1).

L26 ANSWER 8 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1964:410723 CAPLUS
DOCUMENT NUMBER: 61:10723
ORIGINAL REFERENCE NO.: 61:1707c-f
TITLE: Separation of several groups of alkaloids with the use of thin-layer chromatography
AUTHOR(S): Kamp, W.; Onderberg, W. J. M.; van Seters, W. A.
CORPORATE SOURCE: Rijksuniv., Utrecht, Neth.
SOURCE: Pharmaceutisch Weekblad (1963), 98(22), 993-1007
CODEN: PHWEAW; ISSN: 0031-6911
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
IT **850-57-7**, Thebaine, hydrochloride
(chromatography of)
RN 850-57-7 CAPLUS
CN Morphinan, 6,7,8,14-tetradehydro-4,5-epoxy-3,6-dimethoxy-17-methyl-, hydrochloride, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

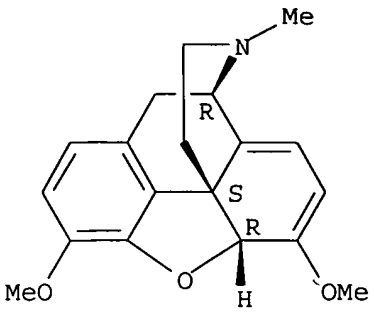


● HCl

AB Silica gel G (Merck) and the ascending **method** was used. The alkaloids were separated as free **bases** or salts and detected with ultraviolet light, Dragendorf reagent. KI-I in HCl, concentrated H2SO4, and N FeCl3. A mixture of atropine, hyoscyamine, scopolamine, strychnine, tetracaine, and veratrin was separated with 9:1 CHCl3-Et2NH. Addition of 10%MeOH or 10% cyclohexane to the mobile phase gave a better separation The spots were detected with Bouchardat reagent (Pinxteren and Verloop, CA 56, 10287c). Separation of quinine carbonate (I), cinchonidine (II), cinchonine (III), quinine ethyl carbonate (IV), hydroquinine (V), quinidine (VI), and quinine (VII) was tried. With 9:1 CHCl2-EtOH or 9:1 CHCl3-Et2NH, only I and IV, were separated With 1:1 CHCl3-BuOH saturated with 10% NH4OH, I, IV, and V, were separated By a two-dimensional procedure with 1:1 CHCl3-BuOH saturated with 10% NH4OH in the 1st direction 23:9:9 and kerosine-Et2NH-Me2O in the 2nd direction, the plates being dried at 150°C. and then sprayed with Dragendorf-Munier reagent, 6 spots were developed (I, II and VI, III, IV, V, and VII). Using the same two solvents as above, some fluorescent alkaloids were separated by a two-dimensional procedure, and spots were obtained for I, IV, rivanol lactate, V, VI, VII, atabrine, and hydrastinine. In another two-dimensional procedure with 4:16:2:1 petr. ether-ether-EtOH-Et2NH as the first solvent and, 40:30:30:2 CCl4-BuOH-MeOH-10% NH4OH as the 2nd solvent, acetyldihydrocodeinone, codeine, hydrocodone bitartrate, hydromorfone, ethylmorphine, oxycodone, heroine, morphine, narcotine, papaverine, and thebaine were separated In a two-dimensional procedure using 40:30:30:1 CCl4-BuOH-MeOH-25% NH4OH and 20:80:1 petr. ether-ether-Et2NH, the following volatile alkaloids were separated: amydricaine, methadone, mepyramine, tripelennamine, Benadryl, cotarnine, methylamphetamine, pethidine, sparteine sulfate, and amylocaine. Caffeine, theobromine, and theophylline was separated with 5:5:1 CCl4-CHCl3-MeOH. Antipyrine, amidopyrine, and 8-hydroxyquinoline sulfate were separated with 20:80:10:1 petr. ether-ether-EtOH-Et2NH and colored with a N FeCl3 solution

L26 ANSWER 9 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1961:133649 CAPLUS
DOCUMENT NUMBER: 55:133649
ORIGINAL REFERENCE NO.: 55:25167b-e
TITLE: Determination of organic **bases** and alkali salts of organic **acids** with a solution of perchloric **acid** in glacial acetic **acid** in a water-free medium
AUTHOR(S): Rink, Melanie; Lux, Rosemarie
CORPORATE SOURCE: Univ. Bonn, Germany
SOURCE: Deutsche Apotheker Zeitung (1961), 101, 911-18
CODEN: DAZEA2; ISSN: 0011-9857
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
IT **115-37-7**, Thebaine
(determination of)
RN 115-37-7 CAPLUS
CN Morphinan, 6,7,8,14-tetradehydro-4,5-epoxy-3,6-dimethoxy-17-methyl-, (5α)- (9CI) (CA INDEX NAME)

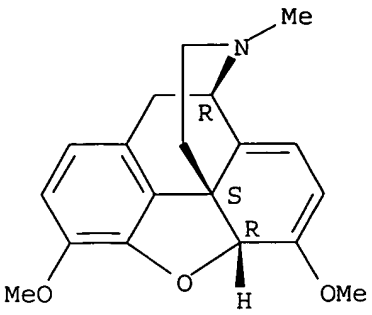
Absolute stereochemistry.



AB Previous work (CA 54, 13550e) is extended. The solvents are AcOH, benzene, Ac2O, and a 3% solution of Hg-(AcO)2 in AcOH, singly or in mixts., with other solvents in certain cases. The titrations are **made** with 0.1N HClO4 in AcOH, with Metanil Yellow, crystal violet, Fast Blue B, Brilliant Green, or malachite green as indicators. Titration curves are given in 16 cases. Tabulations of results are given for 44 compds. The results are very close to theoretical for Na salicylate, saccharin, phenobarbital, barbital, Na p-aminosalicylate, NaOBz, nicotinic **acid**, nikethamide, nicotinamide, isonicotinic **acid** hydrazide, dihydromorphi-none-HCl, dihydrocodeinone bitartrate, dihydrocodeine-HCl, lobeline, codeine, codeine-HCl, choline chloride, thiamine-HCl, pyridoxine-HCl, papaverine, papaverine-HCl, cinchophen, narcotine, narcotine-HCl, hydrocotarnine-HCl, morphine-HCl, ethylmorphine-HCl, dihydrohydroxy-**codeinone**, thebaine, atropine, scopolamine-HBr, meperidine-HCl, yohimbine-HCl, strychnine, veratrine, narceine, pilocarpine-HCl, prostigmine, hydrastinine chloride, choline bitartrate, and choline dihydrogen citrate. Low values found were for caffeine citrate 49, cotarnine chloride 95, and cotarnine phthalate approx. 88% of theoretical. Details of the titrations are given for each compound

L26 ANSWER 10 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1961:29793 CAPLUS
DOCUMENT NUMBER: 55:29793
ORIGINAL REFERENCE NO.: 55:5866g-i,5867a
TITLE: Identification and determination of nitrogenous organic **bases** with ammonium reineckate
AUTHOR(S): Lee, Kum-Tatt
SOURCE: Journal of Pharmacy and Pharmacology (1960), 12, 666-76
CODEN: JPPMAB; ISSN: 0022-3573
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
IT **115-37-7**, Thebaine
(detection and determination of, as reineckate)
RN 115-37-7 CAPLUS
CN Morphinan, 6,7,8,14-tetradehydro-4,5-epoxy-3,6-dimethoxy-17-methyl-, (5α)- (9CI) (CA INDEX NAME)

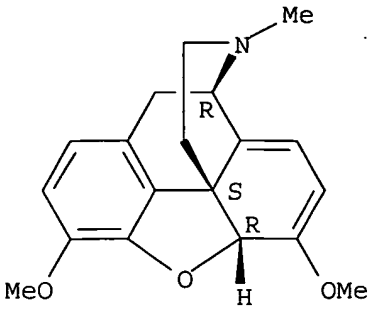
Absolute stereochemistry.



AB Procedures are given for the **preparation** of reineckates of monobasic and mono- and direineckates of dibasic alkaloids, synthetic narcotics, sulfonamides, antihistaminics, and other organic N **bases** with a tabulation of mol. composition of the reineckate, decomposition temperature, E (1 g. mol./l., 1 cm.), and solubility in H2O g./100 ml. at 5° and 27°. Quant. determination is based upon solution of the precipitated reineckate in Me2CO and reading at 525 mμ. The amount of **base** or its salt is calculated for compds. which form monoreineckates from the equation w = A/106.5 + v/1000 + M, and for compds. which form direineckates w = A/213.0 + v/1000 + M, where w = weight of **base** or salt in mg., A = observed optical d., v = volume of Me2CO used, and M = mol. weight of **base** or salt. Passage of Me2CO solns. of reineckates through a column (1 cm. + 10 cm.) of Permutit De-Acidite FF resin, treated with 50 ml. 0.5N NaOH then washed with H2O to pH 7, allowed recovery of the conjugate **base** in the Me2CO eluate. Ultraviolet absorption curves (2 mg. in 100 ml. 95% EtOH) are given for **bases** and reineckates of strychnine, morphine, and pethidine; the reineckate and HCl salt of pecazine; also for thonzylamine mono-reineckate and HCl salt, sulfamerazine and sulfathiazole reineckates and **bases**, and phenindamine reineckate and tartrate.

L26 ANSWER 11 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1956:82134 CAPLUS
DOCUMENT NUMBER: 50:82134
ORIGINAL REFERENCE NO.: 50:15554a-i,15555a-i,15556a-i,15557a-i,15558a-i,15559a
TITLE: **Synthesis** of morphine
AUTHOR(S): Gates, Marshall; Tschudi, Gilg
CORPORATE SOURCE: Univ. of Rochester, Rochester, NY
SOURCE: Journal of the American Chemical Society (1956), 78, 1380-93
CODEN: JACSAT; ISSN: 0002-7863
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
OTHER SOURCE(S): CASREACT 50:82134
IT **115-37-7**, Thebaine
(derivs., in morphine **synthesis**)
RN 115-37-7 CAPLUS
CN Morphinan, 6,7,8,14-tetradehydro-4,5-epoxy-3,6-dimethoxy-17-methyl-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI For diagram(s), see printed CA Issue.

AB The completion of the 1st **synthesis** of morphine is described. The yield of 3,4-dimethoxy-9,10-dioxo-4b-cyanomethyl-4a,4b,5,8,9,10-hexahydrophenanthrene (I), m. 238-40°, **prepared** by the **method** described previously (C.A. 45, 1089c), was raised to 66% by the use of purified dioxane instead of AcOH as solvent, heating for 3 days, and using (cyanomethyl)quinone recrystd. from Me2CO. I (1.00 g.) hydrogenated 4 hrs. at 27 atmospheric pressure in 20 cc. absolute EtOH over 200 mg. Cu chromite catalyst at 124-31°, the cooled mixture diluted with C6H6, filtered with celite, washed with 10% NaOH, 1% HCl, and H2O, dried, concentrated, and the residue recrystd. gave 504 g. oxo lactam (II) (R = H), colorless small prisms, m. 264-6° (all m.ps. corrected), readily soluble in 12N HCl and repptd. unchanged on dilution The 6-Cl derivative of I (586 mg.) gave similarly 83 mg. II (R = Cl), m. 268-9°, soluble in 12N HCl and repptd. on dilution II (801 mg.) added to 4.5 g. KOH pellets and 8 cc. 100% N2H4.H2O at 155°, the mixture heated 1 hr. at 155°, cooled, and diluted with 4 vols. H2O gave 703 mg. lactam (III), m. 209.5-11°, felty needles from cold C6H6 and prisms from hot C6H6. If the reduction of II is carried out similarly at 200-10°, a mono-Me ether, C17H19NO3, m. 283-6° (uncor.), is obtained; this was readily remethylated with Me2SO4 and alkali to III; the crude reaction mixture remethylated yielded 56% III. III (150 mg.) in 50 cc. PhMe concentrated to 25 cc. by boiling, treated with 15 mg. NaH, refluxed 135 min., treated with 1 cc. MeI, the mixture refluxed 1 hr., cooled, washed, and concentrated gave 131 mg. N-Me derivative (IV) of III, m. 227-9° (from C6H6), soluble in 12N HCl, repptd. unchanged on dilution III (505 mg.) in 40 cc. PhMe concentrated to about 20 cc. by boiling, refluxed 2 hrs. with 45 mg. NaOH, cooled, treated with 1 cc. MeI, refluxed 1 hr., concentrated to about 10 cc., diluted with 12 cc. dry Et2O, treated with 15 cc. N LiAlH4 in Et2O, refluxed 48 hrs., decomposed with EtOAc, treated with dilute HCl, the organic layer extracted with dilute HCl containing a little NaHSO3, the combined aqueous layer and extract slowly run into excess strong aqueous KOH containing Rochelle salt, extracted with Et2O, the extract dried, evaporated, heated in vacuo at 100°, and the residual viscous oil dissolved in a small amount of MeOH and treated with 425 mg. picric **acid** in MeOH yielded 780 mg. picrate (V) of racemic β-Δ6-dihydrodeoxycodeine Me ether (VI), bright yellow crystals, m. 199.5-200.5° (decomposition). IV reduced similarly with LiAlH4 gave 82% V. V (280 mg.) partitioned between dilute aqueous LiOH and Et2O, and the Et2O layer washed, dried, and evaporated yielded 156 mg. VI, large colorless

plates or leaves m. 84-5° (from MeOH). VI (11 mg.) treated with 14 mg. racemic dibenzoyltartaric **acid** in MeOH gave the racemic dibenzoyl tartrate (VII), m. 184-4.2° (from MeOH-CHCl3). Racemic VI (120 mg.) in MeOH treated with 159 mg. dibenzoyl-L(+)-tartaric **acid** in MeOH yielded 111 mg. dibenzoyl-L(+)-tartrate (VIII) of d-VI, colorless prisms, m. 162-3.5° (from MeOH), [α]D27 44.5° (c 1.53, CHCl3). VIII (57 mg.) in H2O treated with excess dilute NH4OH gave 22 mg. d-VI, m. 43.5-4.5° (from pentane), [α]D27 80° (c 1.24, EtOH), also obtainable in a modification, m. 57.5-58°. d-VI and MeI gave d-VI.MeI, m. 186.5-88° (from MeOH-EtOAc). d-VI gave the picrate, m. 230-1.5° (decomposition). The MeOH filtrates from the crystallization of the VIII concentrated to dryness, treated with dilute NH4OH, allowed to stand overnight, the viscous oil washed with H2O by decantation twice, dried, dissolved in MeOH, and the solution treated with 82 mg. dibenzoyl-D(-)-tartaric **acid** yielded 70 mg. dibenzoyl-D(-)-tartrate (IX) of l-VI, m. 161.5-62°, [α]D27 -44° (c 1.94, CHCl3). IX (116 mg.) in H2O basified with NH4OH and triturated gave 48 mg. l-VI, m. 55.5-57° (from MeOH), [α]D27 -79° (c 1.09, EtOH); picrate, m. 228.5-30°. The picrates of l-VI and d-VI (2.15 mg. each) crystallized from CHCl3-MeOH gave V, m. 210-12°. β-Thebainone (X) HClO4 salt (50 mg.), m. 150-3° (evacuated tube), in 1.5 l. EtOH hydrogenated under ambient conditions 45 min. over 500 mg. PtO2, the mixture acidified with 20 cc. concentrated HCl, hydrogenated 50-60 hrs., filtered, the filtrate concentrated, filtered from the crystalline deposit, the filtrate evaporated to dryness on the steam bath in an air stream, the combined residues suspended in 10% aqueous NaOH containing some Na2S2O4, and the insol. portion washed with H2O and resuspended in 10% aqueous NaOH left 2.5 g. β-tetrahydrodeoxycodeine (XI) hemihydrate, m. 140-52° with sintering at 126° (from EtOAc), [α]D29 -40° (c 1.24, CHCl3); XI.HI, m. 259-61° (decomposition); XI.MeI.H2O, m. 160-4° with softening at 150° (from MeOH-EtOAc); XI picrate, m. 233-4° (decomposition). The combined alkaline filtrates from the XI carbonated to excess, extracted with CHCl3, and the extract worked up yielded 19.2 g. β-dihydrothebainol (XII), m. 165.5-66°, [α]D30 -23° (c 0.920, EtOH); 2nd crop, 1.5 g. XII.MeI, m. 264-5° (from MeOH-EtOAc). β-Dihydrothebainone (XIIa) (6.18 g.) [purified through the HClO4 salt, m. 262-4° (decomposition)] methylated with PhNMe3OEt gave 6.31 g. alkali-insol. redbrown glass which, distilled in a mol. still at 10-2 mm. at 220-30°, yielded 5.55 g. Me ether (XIII) of XIIa, m. 122-3°, [α]D27 -51.4° (c 2.49, EtOH) (from cyclohexane); picrate, m. 249-50° (decomposition) (from CHCl3-MeOH); semicarbazone-0.5EtOH, colorless cottony needles, m. 202.5-204° (with gas evolution). XIII (132 mg.) in 4 cc. dry Et2O treated with 2 cc. 0.56M LiAlH4 in Et2O, the mixture allowed to stand 1 hr., decomposed with EtOAc, then with excess dilute HCl, the clear **acid** solution run into excess aqueous KOH containing Rochelle salt, the separated oily **base** worked up with CHCl3, and the crude material treated with picric **acid** gave a picrate, m. 181-3°; the crude material treated with hot cyclohexane and seeded gave 45 mg. Me ether (XIV) of XII, prisms, m. 152-4°; the combined filtrates concentrated, and the residue treated with MeOH and 70 mg. picric **acid** yielded 63 mg. picrate (XV) of the C6-epimer (XVI) of XIV, prisms, m. 224.5-26° (decomposition). XV (259 mg.) partitioned between dilute aqueous LiOH and CHCl3, and the CHCl3 layer worked up gave 159 mg. pale yellow glass which, distilled at 10-2 mm. and 160-200° bath temperature, gave a noncrystallizable colorless distillate of XVI, [α]D27

-19° (c 2.25, EtOH); XVI.MeI, m. 146-51° with gas evolution (from EtOAc-MeOH). PhNMe2-p-MeC6H4SO3Me-adduct (17.5 g.) in 40 cc. warm absolute EtOH added to 1.4 g. Na in 20 cc. warm absolute EtOH, the precipitate filtered off, washed with absolute EtOH, the combined filtrates treated with 13.0 g. XII, the EtOH removed in vacuo, the dark residue heated 1.5 hrs. at 130°, cooled, dissolved in 15% AcOH, steam-distilled to remove the PhNMe2, basified with 20% KOH, extracted with CHCl3, and the extract washed, dried, and evapd gave 10.3 g. XIV, m. 153-5°, [α]D27 -22° (c 2.50, EtOH); XIV.MeI, small colorless prisms, m. 243-5° (from EtOAc-MeOH); XIV picrate, 2 polymorphic forms, m. 190-1°, 221-2.5°. XIV (10.3 g.), m. 149-51°, in 95 cc. dry pyridine kept 5.5 days with 12.5 g. p-MeC6H4SO2Cl, cooled, diluted with 20 cc. H2O, allowed to stand 2 hrs., diluted with ice water, just basified with aqueous Na2CO3, extracted with Et2O, and the extract worked up yielded 16.4 g. p-toluenesulfonate (XVII) of XIV, colorless needles, m. 133-3.5° (from EtOAc-Et2O). Crude XVII (16.4 g.) refluxed 2 hrs. in s-collidine, cooled, diluted with Et2O, washed with dilute aqueous Na2CO3 and H2O, evaporated, the residue steamdistd. to remove the collidine, diluted with Et2O, separated from a small aqueous layer (which was extracted with Et2O), evaporated, and the thick colorless oily residue (9.8 g.) chromatographed on 550 g. Al2O3 gave 5.30 g. crude d-VI, m. 54-6°, and 4.35 g. crude Δ5-isomer (XVIII) of d-VI, partially crystalline Each crude material purified through the picrates yielded 8.55 g. picrate (XIX) of d-VI, m. 230-2° (decomposition), and 4.60 g. crude picrate of XVIII, m. 225.5-6.5° (decomposition). XIX partitioned between CHCl3 in aqueous LiOH in the usual manner yielded 4.85 g. d-VI, m. 43.5-44° or 57.5-58°, both colorless needles from pentane, [α]D27 80° (c 1.55, EtOH). l-VI and d-VI (11 mg. each) combined and recrystd. from MeOH yielded 19 mg. VI, m. 82.5-84°. d-VI.MeI, m. 188-9° (from MeOH-EtOAc); VIII, m. 163-3.5°, [α]D27 48° (c 1.80, CHCl3). VIII (1.35 mg.) and 1.33 mg. XIII combined and recrystd. from MeOH gave VII, m. 184°. d-VI (50 mg.), m. 57-7.5°, hydrogenated in MeOH containing AcOH over PtO2, filtered, concentrated, the residue diluted with Et2O, washed with excess dilute NH4OH and H2O, dried, concentrated, and the residue dissolved in a little MeOH and treated with 40 mg. picric **acid** in MeOH yielded 91 mg. picrate (XX) of the Me ether (XXI) of XI, m. 204-6° (from CHCl3-MeOH). XX (61 mg.) partitioned between Et2O and dilute LiOH gave 35 mg. XXI, colorless crystals, m. 36.5-7.5°, [α]D27 -18° (c 1.92, EtOH); XXI.MeI, m. 236-7° (from EtOAc-MeOH). The picrate of XVIII similarly treated yielded 2.60 g. XVIII, colorless prisms or plates, m. 78.5-79° (from pentane); XVIII.MeI, colorless plates or prisms, m. 227.5-29° (from MeOH-EtOAc); dibenzoyl-L(+)-tartrate of XVIII, m. 166-6.5° (from MeOH). XVIII hydrogenated in the usual manner yielded XXI, m. 36.5-7.5°; XXI picrate, m. 201-2°; XXI.MeI, m. 235-6°. XII (2.11 g.), m. 163-6°, in 25 cc. absolute EtOH treated with CH2N2 from 9.0 g. H2NCON(NO)Me (XXII), kept 23 hrs. at room temperature, evaporated to dryness, the residue dissolved in 1:1 C6H6-hexane solution, extracted with Claisen alkali, washed, dried, concentrated, and the residual orange viscous oil or glass (1.66 g.) treated in Me2CO with HBr gave the cis isomer (XXIII).HBr of XIV.HBr, m. 254.5-55° (from Me2CO-MeOH),

[α]D28 34° (c 0.44, EtOH). XXIII.HBr partitioned between aqueous Na2CO3 and Et2O gave noncrystallizable XXIII, [α]D27 -28.4° (c 1.52, EtOH); XXIII.MeI, colorless fine needles, m. 279-81° (from MeOH). XXIII (0.69 g.) in 8 cc. dry pyridine kept 4.5 days at room temperature with 1.00 g. p-MeC6H4SO2Cl, and the mixture worked up in the usual manner gave 0.95 g. p-toluenesulfonate (XXIV) (ring II/III cis) of XXIII, sheaves or prismatic needles, m. 165-6° (from Me2CO-EtOAc). Crude XXIV (0.90 g.) refluxed 2.5 hrs. in 10 cc. collidine, cooled, diluted with Et2O, washed with aqueous Na2CO3, steam-distilled, the residue dissolved in 1% HCl, washed with Et2O, basified with Na2CO3, extracted with CHCl3, the extract worked up, and the residue distilled at 0.001 mm. and 140-80° yielded 0.47 g. Δ5(or 6)-dihydrodeoxycodeine Me ether (XXV), nearly colorless viscous oil. XXV (48 mg.) in a very small amount of MeOH treated with 35 mg. fumaric **acid** and diluted with absolute Et2O yielded 74 mg. fumarate (XXVI) of XXV, m. 233-5° with gas evolution (from MeOH-Et2O). XXVI (92 mg.) partitioned between aqueous Na2CO3 and Et2O yielded 57 mg. XXV, colorless, very viscous oil; XXV.MeI, m. 251.5-2.5° (from Me2CO-EtOAc). XXV (598 mg.) and 244 mg. BzOH in 14 cc. CHCl3 treated 3 hrs. with 10.6 cc. 0.583M BzO2H in CHCl3, the mixture extracted with aqueous Na2CO3, then with aqueous Na2S2O4, dried, evaporated, and the residue triturated with cyclohexane yielded 503 mg. epoxide (XXVIa) of XXV, amorphous solid, m. 80-170°; the cyclohexane filtrate concentrated gave 180 mg. yellow glass which yielded 128 mg. picrate (XXVII) of XXVIa, small bright yellow prisms, m. 198.5-200°. XXVII (100 mg.) partitioned between CHCl3 and aqueous dilute LiOH yielded 57 mg. XXVIa, m. 92-3.4°. The crude, cyclohexane-insol. XXVIa hydrogenated catalytically yielded 34% XXVII, and thus probably contained the corresponding N-oxide. The crude total XXVIa from 200 mg. XXV in dry Et2O kept 2 days at room temperature with 4 cc. 0.95M LiAlH4, decomposed with HCl, the aqueous acidic layer added dropwise to strong aqueous KOH containing Rochelle salt, extracted with CHCl3, the extract worked up, and the residual oil (120 mg.) chromatographed on 30 g. Al2O3 gave 55 mg. material which with 42 mg. picric **acid** in MeOH yielded 51 mg. picrate, m. 198-200° (decomposition); the picrate partitioned between dilute aqueous LiOH and Et2O gave 14.5 mg. 7-HO derivative (XXVIII) of XXI, heavy prisms, m. 141-2° (from EtOAc); XXVIII.MeI, m. 262-3.5° (from EtOAc-MeOH); XXVIII picrate, m. 218-19° (decomposition) (from MeOH). XXV (89 mg.) in 1 cc. C6H6 treated with 1.6 cc. 0.198M OsO4 in C6H6 1.5 hrs. at room temperature, the precipitate centrifuged, washed with C6H6, warmed on the steam bath with aqueous Na2SO3 and Na2HPO4, filtered, the black residue washed with MeOH, the combined filtrates basified with NH4OH, extracted with CHCl3, and the extract worked up gave 71 mg. pale yellow glass, which with 50 mg. picric **acid** in MeOH yielded 54 mg. picrate (XXIX) of cis-6;7-dihydroxy-β-tetrahydrodeoxycodeine Me ether (XXX), bright yellow needles, m. 226-7° (decomposition) (from MeOH-CHCl3). XXIX (63 mg.) partitioned between aqueous LiOH and CHCl3 yielded 39 mg. XXX, colorless plates, m. 151-2° (from EtOAc). XXV (382 mg.) in 6 cc. 98% HCO2H treated 40 hrs. at room temperature with 0.20 cc. 30% H2O2, diluted with H2O, basified with 10% aqueous NaOH, extracted with CHCl3, the extract worked up, the residue dissolved in NaOH in MeOH, the MeOH removed, the residue partitioned between CHCl3 and H2O, and the CHCl3 layer worked up gave 302 mg. transisomer (XXXI) of XXX, colorless needles, m. 201-2°; picrate, m. 245-6.5° (decomposition) (from MeOH). XXVIa in MeOH hydrogenated gave the mono-Me ether of XXXI, m. 174.5-5.5°, large prisms from EtOAc, as a by-product. XXV (208 mg.) in 18 cc. 18%

H2SO4 heated 5 days under N on the steam bath, diluted with H2O, basified with aqueous KOH, extracted with CHCl3, and the extract worked up yielded 228 mg.
very viscous oil or glass which, chromatographed on 13 g. Al2O3, gave 110 mg. crude XXV (identified as VIII, 216 mg., m. 163.5-65°), an intermediate fraction which, rechromatographed and processed through its picrate [21 mg., m. 214-16.5° (decomposition)], yielded 7 mg. XXVIII, m. 140-1° [XXVIII.MeI, m. 262-3.5°], and 58 mg. XIV, stout colorless prisms, [α]D28 -23° (c 2.78, EtOH), m. 151-3.5° [XIV.MeI, m. 243-4°]; in some runs small amts. of XVI were recovered as its picrate, m. 216-22°. VI (98.5 mg.) gave similarly 28% dl-XIV, colorless small prisms, m. 149-50.5°. The hydration of VI gave small amts. of dl-XXVIII, fine colorless prismatic needles or blades, m. 172.5-3.5°. XIV (300 mg.), m. 153-4°, 10 cc. (HOCH2-CH2)2O, 12 pellets KOH, and 0.2 cc. N2H4.H2O heated 1.25 hrs. under N at 221-7° (the mixture blown with N during the 1st 5 min.), cooled, diluted with H2O containing a little Na2S2O4, carbonated to excess, extracted with CHCl3, and the extract worked up gave 186 mg. slowly crystallizing residue; the aqueous layer extracted with BuOH, the extract worked up, the residue in MeOH treated overnight with CH2N2 in Et2O (from 1 g. XXII), the mixture evaporated, the residue partitioned between CHCl3 and dilute NH4OH, the CHCl3 layer worked up, and the residue (90 mg.) chromatographed on 15 g. Al2O3 gave 97 mg. XIV, m. 152.5-54° (from EtOAc), and 105 mg. XII, m. 165.5-66° (from EtOAc), [α]D28 -25° (c 1.06, EtOH) (soluble in alkali and repptd. by CO2) (XII.MeI, m. 266-8°). XVI (125 mg.) cleaved gave dl-XII, colorless leaves, m. 185-6°. XVI (204 mg.) and 247 mg. pyridine HCl salt heated 4 hrs. at 195-200°, cooled, dissolved in H2O, basified with KOH containing Na2S2O4, and extracted with CHCl3, the aqueous alkaline layer carbonated to excess, extracted with BuOH, and the extract worked up gave 72 mg. compound, C17H21NO2, small prisms, m. 258-62° (decomposition), [α]D28 46° (c 1.32, dioxane); it had lost both MeO groups and the OH group at C-6. K (380 mg.) in 7 cc. absolute Me3COH and 20 cc. dry C6H6 distilled with the addition of more C6H6 until the b.p. of pure C6H6 was reached, the mixture refluxed 10 min., treated with 400 mg. XII, m. 162-4°, and 3 g. Ph2CO in dry C6H6, refluxed 2.5 hrs., cooled, extracted with dilute HCl, the **acid** extract washed with C6H6, basified with NH4OH, extracted with CHCl3, and the extract worked up yielded 399 mg. light tan glassy residue which, dissolved in EtOH and treated with excess 25% HClO4, gave 450 mg. X.HClO4, m. 264-6° (decomposition) (from EtOH); 2nd crop, 25 mg. X.HClO4 partitioned between CHCl3 and dilute NH4OH gave X, m. 120.5-22° (from aqueous MeOH), [α]D26 -47° (c 1.53, EtOH); oxime, m. 223-5° (decomposition). X (301 mg.) in 30 cc. 1:1 AcOH-dry Et2O containing a few drops 4N HBr in AcOH treated with 3 cc. of a solution of 1.60 g. Br in 10 cc. glacial AcOH, the mixture kept 22 hrs. at room temperature, diluted with H2O, just basified with dilute NH4OH, extracted with CHCl3, the extract worked up, and the residue triturated with EtOAc gave 1,x,x-tribromo-β-dihydrothebainone (XXXII), small prisms, m. 219-21° (decomposition), [α]D25 -53.2° (c 3.18, CHCl3). XXXII (134 mg.) in AcOH hydrogenated over PtO2 gave the 1-Br derivative (XXXIII) of XIIa, m. 172.5-74°, [α]D26 -32° (c 2.03, EtOH); XXXIII.HClO4, m. 272-6° (decomposition), [α]D25 -12° (c 1.25, 50% aqueous EtOH); XXXIII 2,4-dinitrophenylhydrazone, m. 144-8° with gas evolution (from EtOAc-CHCl3). X.HClO4 (402 mg.) partitioned between NH4OH and CHCl3, the resulting free X dissolved in 10 cc. glacial AcOH, the solution treated with 0.002 moles Br in 8 cc. glacial

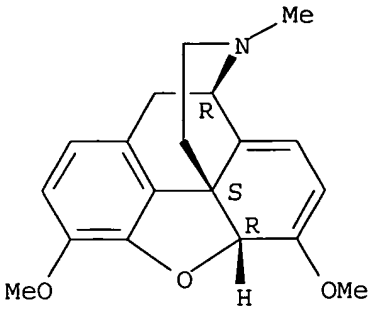
AcOH, kept 24 hrs. at room temperature, treated with 220 mg. 2,4-(O2N)2C6H3NHNH2 (XXXIV), refluxed 5 min., cooled, basified with NH4OH, extracted with CHCl3, the extract worked up, and the orange-red residue (704 mg.) chromatographed on 15 g. Al2O3 gave 229 mg. 2,4-dinitrophenylhydrazone (XXXV) of cis-1-bromothebainone (XXXVI), m. 207-8° (from EtOAc), [α]D27 -1307° (c 1.63, CHCl3), -1090° (c 0.800, Me2CO).

Thebainone hemihydrate (103 mg.) and 70 mg. XXXIV in 3 cc. glacial AcOH heated 20 min. on the steam bath, cooled, treated with 100 mg. NaOAc, brominated 5 min. with 3.33 cc. solution of 1.60 g. Br in 100 cc. AcOH, diluted with H2O, basified with NH4OH, extracted with CHCl3, and the extract worked up gave 88 mg. XXXV, orange plates, m. 207-8°. β-Thebainone HClO4 salt converted to the 2,4-dinitrophenylhydrazone, m. 224-5°, and a 63-mg. portion in 1 cc. glacial AcOH containing 15 mg. NaOAc brominated with 1.32 g. of a solution of 1.60 g. Br in 100 cc. AcOH yielded 74 mg. 1-bromo-β-thebainone 2,4-dinitrophenylhydrazone (XXXVII), ruby-red prisms, m. 157-65° with gas evolution, [α]D27 -76.4° (c 1.57, CHCl3). XXXVII (34 mg.) heated 2.5 hrs. in 1 cc. glacial AcOH on the steam bath, diluted, basified with NH4OH, extracted with CHCl3, and the extract worked up yielded XXXV, orange-yellow plates, m. 206-7° (from EtOAc). XXXV (200 mg.) in 20 cc. Me2CO and 8 cc. 12N HCl refluxed 20 min., cooled, diluted with H2O, extracted with CHCl3, the extract washed with dilute NH4OH, dried, concentrated to 25 cc., evaporated, and the residue partitioned between 30% AcOH and 1:1 C6H6-cyclohexane yielded 13 mg. XXXV, m. 203.5-205°, [α]D25 -1360° (c 0.0472, CHCl3); the aqueous layer basified with NH4OH, extracted 4 times with CHCl3, and the extract worked up gave 76 mg. XXXVI, small colorless needles, m. 198.5-9.5°, [α]D27 -85° (c 1.54, CHCl3), readily soluble in dilute alkalies with yellow color, also obtained by treating 31 mg. thebainone hemihydrate in 1 cc. AcOH with 1 cc. solution of 1.60 g. Br in 100 cc. AcOH. XXXVI (298 mg.), m. 195-7°, in 10 cc. AcOH treated with 3 cc. AcOH containing 0.79 millimole Br, then dropwise with 4N HBr in AcOH, diluted with H2O, just basified with NH4OH, extracted with CHCl3, and the residue from the extract treated with Me2CO yielded 1.77 mg. 1,x-dibromothebainone (XXXVIII), m. 215-18° (decomposition) (from CHCl3-Me2CO); it did not give a precipitate with alc. AgNO3 and was unaltered by short boiling with collidine; it was slowly soluble in cold 15% aqueous KOH and this solution warmed deposited an amorphous solid. Thebainone hemihydrate (308 mg.) dibrominated gave 355 mg. XXXVIII (without added HBr in AcOH). XXXVI (174 mg.) in 15 cc. EtOH hydrogenated 11 min. over 21 mg. PtO2, the mixture filtered, diluted with H2O, basified with NH4OH, and worked up with CHCl3 gave 191 mg. cis-1-bromodihydrothebainone (XXXIX), m. 99-115°, foaming, resolidifying, and remelting at 154-62°; purified through XXXIX.HI, colorless needles m. 206.5-8.5° (from H2O), crumbled on drying at 100°; XXXIX.HBr.2H2O, m. 202-6°, foaming 210-12°, loss of hydrate H2O at 140-60°, [α]D26 -48.6° (c 1.07, EtOH). XXXVI (96 mg.) in EtOH hydrogenated over 200 mg. Pd-BaCO3 yielded 74 mg. crude cis-XIIa.0.5H2O, m. 123-36°, converted to cis-XIIa.HI, m. 277-8.5°; XIIa.HI with dilute NH4OH gave cis-XIIa, heavy colorless prisms, m. 123-52°; oxime, m. 252-3.5°. XXXIX.HBr.2H2O (497 mg.) in 10 cc. glacial AcOH treated dropwise with swirling with 7 cc. glacial AcOH containing 0.002 mole Br, kept 15 min. at room temperature, treated with 220 mg. XXXIV, allowed to stand 1 hr., treated with 164 mg. NaOAc, allowed to stand 23 hrs., concentrated to dryness in vacuo, the residue refluxed 0.5 hr. in 10 cc. purified pyridine, the pyridine removed in vacuo, the

residue in CHCl3 washed with 10% aqueous NaOH and H2O, dried, evaporated, and the residue chromatographed with CHCl3 on 25 g. Al2O3 gave 276 mg. 2',4-dinitrophenylhydrazone (XL) of 1-bromocodeinone (XLI), orange prismatic needles, m. 224-5°, [α]D27 -1968° (c 0.064, CHCl3). XL (200 mg.) refluxed 20 min. with 20 cc. Me2CO and 12 cc. 12N HCl, diluted with H2O, extracted with CHCl3, the CHCl3 extract worked up in the usual manner, the residue partitioned between 50% aqueous AcOH and 1:1 C6H6-cyclohexane, and the **acid** layer processed yielded 32 mg. unchanged XL, m. 219-22°; the colorless **acid** solution cooled with ice, treated with excess 10% aqueous NaOH, extracted with Et2O, the extract worked up, and the residue (48 mg.), m. 90-2°, moistened with EtOAc altered form and gave crystals of XLI, m. 185-95°; the low-melting form recrystd. from EtOAc yielded XLI, colorless needles, m. 201-2° (decomposition), [α]D26 -182.7° (c 1.42, CHCl3). 1-Bromocodeine (1.54 g.), m. 158-61°, oxidized by the **method** of Homeyer and De LaMater (C.A. 48, 13733a) yielded 1.00 g. pure XLI, m. 202.5-3.5°, [α]D25 -180.6° (c 1.30, CHCl2); 2,4-dinitrophenylhydrazone, m. 224-4.5° (from EtOAc). XLI (86.4 mg.) in 5 cc. EtOH hydrogenated over 15 mg. PtO2 yielded 19 mg. 1-bromodihydrocodeinone, m. 207.5-8.5° (from EtOAc) (chromatographed on 3.0 g. Al2O3). XLI (200 mg.), m. 202.5-3.5°, 0.5 g. LiAlH4, and 30 cc. tetrahydrofuran refluxed 46 hrs., treated with EtOAc, acidified with 2N HCl, extracted with Et2O, the **acid** layer added slowly to strong aqueous KOH containing Rochelle salt, extracted with CHCl3, and the extract worked up gave 146 mg. colorless glass which was converted with HBr to 110 mg. codeine (XLII) HBr salt, m. 148-50°, resolidifying and remelting at 273-8°. XLII.HBr in warm H2O with NH4OH gave 70 mg. solid, m. 153-6°, which, recrystd. from aqueous MeOH, yielded 59 mg. XLII, large prisms (hydrated), m. 156.5-58°, [α]D27 -137° (c 1.15, EtOH). XLII, demethylated by the **method** of Rapoport, et al. (C.A. 47, 590g), yielded 34% morphine, colorless needles, m. 254-6.4°, [α]D27 -126° (c 2.32, MeOH).

L26 ANSWER 12 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1956:27991 CAPLUS
DOCUMENT NUMBER: 50:27991
ORIGINAL REFERENCE NO.: 50:5692e-i,5693a-e
TITLE: The morphine-thebaine group of alkaloids. III. The structure of the codeimethines, and related topics
AUTHOR(S): Bentley, K. W.; Thomas, A. F.
CORPORATE SOURCE: Oxford Univ., UK
SOURCE: Journal of the Chemical Society, Abstracts (1955) 3237-44
CODEN: JCSAAZ; ISSN: 0590-9791
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
IT **115-37-7**, Thebaine
(compds. related to)
RN 115-37-7 CAPLUS
CN Morphinan, 6,7,8,14-tetradehydro-4,5-epoxy-3,6-dimethoxy-17-methyl-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



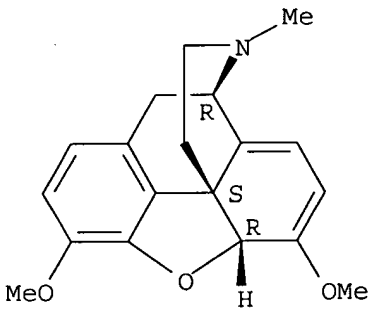
GI For diagram(s), see printed CA Issue.

AB cf. C.A. 47, 1166e. A solution of α-codeimethine (I) (10 g.) [**prepared** from codeine methiodide, m. 118.5°; perchlorate, m. 183°, [α]D20 -116.4° (H2O)] in 100 ml. alc. was neutralized to litmus with HCl, boiled with Raney Ni 2 hrs., the solution filtered, and 5 ml. HClO4 added to precipitate dihydrocodeinone methine perchlorate, colorless plates, m. 267° (from 50% alc.). The noncryst. **base** was characterized as the methiodide, m. 282°. From the mother liquors of the perchlorate was obtained dihydrocodeine methine perchlorate. Na (2 g.) added in slices to a solution of 5 g. I in 350 ml. liquid NH3 and 50 ml. alc. with vigorous stirring, the mixture poured into 250 ml. H2O, saturated with NH4Cl, extracted with ether, and the dried extract evaporated yielded a viscous oil which with 60% HClO4 in alc. gave codeine dihydromethine perchlorate, needles, m. 210° (from aqueous alc.), [α]D -33.4° (H2O); the **base** (II), an oil, was converted into the methiodide, m. 265° (from aqueous alc.). From the mother liquors of the perchlorate was obtained the **base** deoxydihydrocodeine-C-dihydromethine (III), plates, m. 158° (from light petroleum or ether), [α]D 21.5° (CHCl3) (cf. Cahn, C.A. 21, 247), soluble in alkali (the alkaline solution gave an intense red color with diazotized sulfanilic **acid**), gave a green-blue color with FeCl3. Codeine methiodide was reduced as above to give II and III. Reduction in the same manner of β-codeimethine (IV) gave neopine dihydromethine, prisms from light petroleum, m. 88-9°, [α]D -105° (alc.) (cf. B. and Wain, C.A. 47, 1166g). The results of these reductions favored structure I for α-codeimethine and confirmed that for β-codeimethine [cf. Robinson, Nature 160, 815 (1947)]. Comparison of the ultraviolet spectra of I and IV with isoeugenol and with dihydrocodeine methine further confirmed these conclusions. Neopine dihydromethine and **dihydrothebaine**-ϕ dihydromethine were assigned the structures V and VI, resp. (cf. B. and W., loc. cit.). V and VI were recovered unchanged when treated with alc. NaOEt at 90-100° for 8 hrs. VI when heated 3 hrs. at 100° with 5N HCl gave no α,β-unsatd. ketone. V methiodide was degraded by the **method** of B. and W. (loc. cit.) to an oil which was chromatographed on activated alumina. Elution with 3:2-4:1 benzene-light petroleum gave methylmorphenol, m. 62° (picrate, m. 119°), with 90% benzene to benzene, a pale yellow oil, colorless after distillation, b0.05 120°, nD20 1.6518, [α]D 0.0°, and with benzene to 4:1 benzene-CHCl3 an amber glass believed to be (+)-1,2,3,4,9,10-hexahydro-3-hydroxy-6-methoxy-4,5-phenanthrylene oxide, b. 170°, strongly dextrorotatory in CHCl3. Neopine-HBr (3 g.), 50 ml. 30% HCO2H and 2 ml. 30% H2O2 were set aside overnight. On neutralization the solution

gave 1-bromoneopine, prisms from aqueous alc., m. 174°, [α]D -42.1° (alc.); H tartrate, m. 248° (decomposition), [α]D 0° (H2O); methiodide, m. 225°, [α]D 0° (H2O). Ultraviolet absorption spectra were given for codeine, II, and Δ9(14)-dihydrocodeimethine.

L26 ANSWER 13 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1954:69490 CAPLUS
DOCUMENT NUMBER: 48:69490
ORIGINAL REFERENCE NO.: 48:12372e-h
TITLE: Physical **methods** for the identification of narcotics. I. B. Common physical constants for identification of ninety-five narcotics and related compounds
AUTHOR(S): Farmilo, Charles G.; Oestreicher, P. M.; Levi, Leo
CORPORATE SOURCE: Dept. Natl. Health and Welfare, Ottawa, Can.
SOURCE: Bull. Narcotics, U.N. Dept. Social Affairs (1954), 6, 7-19
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
IT **115-37-7**, Thebaine
(identification of, and hydrochloride)
RN 115-37-7 CAPLUS
CN Morphinan, 6,7,8,14-tetradehydro-4,5-epoxy-3,6-dimethoxy-17-methyl-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

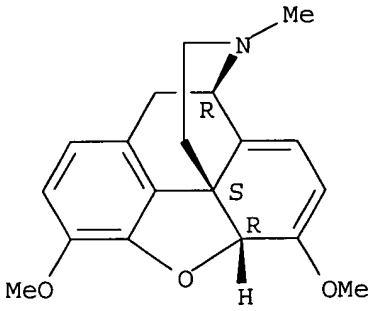


AB Ninety-five narcotics and related compds. were examined by phys. **methods** to determine the validity of this manner of identification. 300-mg. samples of the com. hydrochlorides of ketobemidone, methylketobemidone, oxycodone, cocaine, hydromorphone, pethidine, and d-, l-, and dl-methadones, racemorphan-HBr, and dihydrocodeinone ditartrate were dissolved in a min. volume of water, and the free **bases** precipitated with concentrated NH4OH. Aqueous solns. of metopon, pipidone, ethylmorphine, isomethadone, and phenadoxone-HCl were treated with 2N NH4OH. Hydroxypethidine, α-prodine, benzylmorphine, and diamorphine-free **bases** were **prepared** from aqueous solns. of the HCl salts with dilute NaOH. The solids were washed with cold water and recrystd. twice from 95-100% EtOH, and dried over P2O5 at reduced pressure. The various oils obtained were dissolved in Et2O, the liquid was extracted with Et2O, combined exts. were dried with Na2SO4, volume of Et2O was reduced, the remainder poured into a Spath bulb, washed with dry Et2O, Et2O removed completely at reduced pressure, and oily residue distilled at 0.01-0.1 mm. Hg. M. ps. of pure **bases** were determined by using Fisher-Johns m.-p. block. Water of crystallization and free H2O were determined by a modified Karl

Fischer technique, pKa values were determined by fractional neutralization of salts (Saunders and Srivastava, C.A. 45, 4881g). All phys. data are presented in tabular form. Data obtained from the literature are tabulated. 33 references.

L26 ANSWER 14 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1953:6414 CAPLUS
DOCUMENT NUMBER: 47:6414
ORIGINAL REFERENCE NO.: 47:1168b-i,1169a-e
TITLE: Structure of phenyldihydrothebaine
AUTHOR(S): Bentley, K. W.; Robinson, Robert
CORPORATE SOURCE: Univ. Oxford, UK
SOURCE: Journal of the Chemical Society, Abstracts (1952) 947-57
CODEN: JCSAAZ; ISSN: 0590-9791
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
IT **115-37-7**, Thebaine (and derivs.)
RN 115-37-7 CAPLUS
CN Morphinan, 6,7,8,14-tetradehydro-4,5-epoxy-3,6-dimethoxy-17-methyl-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



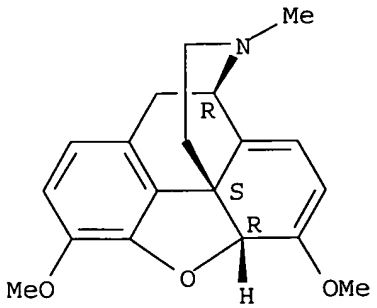
AB The structure of phenyldihydrothebaine (I), deduced from existing data on theor. grounds (R., C.A. 42, 2728e), has been confirmed by oxidation of the **base** to BzH, BzOH, and 4-MeOC6H3(CO2H)2 and by exhaustive methylation of its Me ether to a N-free compound that yields 5,6-(MeO)2C6H3C6H4OMe-5 and the corresponding dialdehyde on oxidation with KMnO4 and the same aldehyde on ozonolysis. I.HClO4 (15 g.) in 100 mL. 2 N NaOH, treated (2 h.) with 75 g. KMnO4 in 1 l. H2O, heated 2 h. on the steam bath (BzH formed during the oxidation), the filtrate and washings concentrated and acidified, give a precipitate (II) and a filtrate (III); II, extracted with H2O, gives BzH; the residue was warmed with NaHCO3, acidified, and the pale brown-gray **acid** was converted into the Cu salt, C20H19O6NCu.2H2O, decomps. above 250°; this may be the salt of 2,4-HO2C(MeO)C6H3CH2CH2NMeCHPhCOCO2H. III, saturated with (NH4)2SO4 and extracted with ether, gives 2.1 g. 4-MeOC6H3(CO2H)2, m. 170°. (+)-α-I.HCl (7 g.) in 100 mL. 10% NaOH, treated with 3.08 mL. Me2SO4 in 8 mL. MeOH and the solid dissolved in warm dilute HClO4, gives (+)-α-phenyl- **dihydrothebaine** Me ether perchlorate, m. 205°, [α]D21 9.26° (H2O); methiodide, m. 205°. (+)-α-Phenyldihydrothebaine methine Me ether-MeI (from 21 g.

base) in 100 mL. MeOH and 12.5 g. Na in 250 cc. MeOH, refluxed 2 h., poured into H2O, saturated with NH4Cl, extracted with ether, and the ether shaken with 2 N HCl, give 15 g. (+)-3,4-dimethoxy-2-(5-methoxy-2-vinylphenyl)stilbene (IV), m. 115°, [α]D18 59° (Me2CO, c 2); the racemate (**prepared** by heating 10 min. at 130°) m. 124°; a small quantity of a very sparingly soluble amorphous polymer, no definite m.p., mol. weight above 5000, is also formed during the heating. IV, shaken with H (3 atmospheric) in AcOEt over Raney Ni, gives (+)-2-(2-ethyl-5-methoxyphenyl)-3,4-dimethoxybibenzyl, b0.1 220°, [α]D18 3.5° (EtOH); partial racemization probably occurs during the distillation IV (1.7 g.) in 25 mL. Me2CO, treated (1.5 h.) with 4.25 g. KMnO4 in 350 mL. warm Me2CO, the residue warmed with dilute Na2CO3, and the filtrate extracted with ether, gives 2,2'-diformyl-5,6,5'-trimethoxybiphenyl (V), isolated as the bis(2,4-dinitrophenylhydrazone), orange-red, m. 277°; the Na2CO3 solution yields 5,6,5'-trimethoxydiphenic **acid** (VI), m. 215°. VI with concentrated H2SO4 (30 min. at 50°) yields 1,5,6-trimethoxyfluorenone-4-carboxylic **acid**, yellow, m. 256° (2,4-dinitrophenylhydrazone, dark red, amorphous, m. 286°). Acetylthebaol, oxidized with CrO3 in cold AcOH, gives 4-acetoxy-3,6-dimethoxyphenanthraquinone (acetylthebaolquinone) (VI), bright yellow, m. 205° (phenazine derivative, C24H18O4N2, yellow, m. 265°). VI (10 g.) in 120 mL. hot AcOH, mixed with 16 mL. 30% H2O2, kept 2 h. at 70-80°, treated with an addnl. 16 mL. H2O2, heated 5 h. at 100°, kept overnight, heated on the water bath, and treated with H2O to incipient precipitation, give a precipitate (VII); further dilution (total volume approx. 1700 mL.) gives 5 g. 6-acetoxy-5,5'-dimethoxydiphenic **acid** (VIII), m. 229°. VIII, heated 30 min. at 50° with concentrated H2SO4, gives 8,3'-dimethoxy-3,4-benzocoumarin (IX), m. 148-9°. VIII (1.5 g.) and 15 mL. 20% NaOH, heated 2 h. on the steam bath, give 6-hydroxy-5,5'-dimethoxydiphenic **acid** (X), m. 172° and then 235° (lactone formation ?); with concentrated H2SO4 (30 min. at 50°) X yields IX. X with Me2SO4 in 20% aqueous NaOH gives VI. VII, shaken with dilute Na2CO3, gives a small quantity of VIII; the insol. portion is regarded as the Ac derivative, very pale brown, m. 192°, of 4'-hydroxy-6,3'-dimethoxy-3,4-benzocoumarin (XI), pale pink, m. 172°, intense blue color with FeCl3. XI (5 g.) in 10.3 mL. boiling 10% KOH, treated (2 h.) with 16.9 mL. Me2SO4 and boiled an addnl. 0.5 h., gives 4.1 g. 5,6,2',5'-tetramethoxy-2-diphenylcarboxylic **acid** (XII), m. 162.5°. XII is unchanged on heating 2 h. on the steam bath with sirupy H3PO4 and P8O6. XII (1 g.), changed into the **acid** chloride with SOCl2 and the CS2 solution refluxed with 0.85 g. AlCl3, gives 1,6-dihydroxy-4,5-dimethoxyfluorenone (or an isomer) (XIII), m. 147°, intense green color with FeCl3. XII (1.2 g.) and 0.83 g. PCl5 in 10 mL. C6H6, warmed on the steam bath, cooled, treated with 1.95 g. SnCl4 in 5 mL. C5H6, kept 6 h. at room temperature, and crystallized from EtOH, give prisms of 1,4,5,6-tetramethoxyfluorenone, bright yellow, m. 183°, intense yellow fluorescence (2,4-dinitrophenylhydrazone, bright red, m. 290°), and needles of XIII (2,4-dinitrophenylhydrazone, m. 285°). IV (5.3 g.) in 30 mL. CHCl3, cooled in ice H2O and treated with O2 containing O3, the ozonide reduced with 20 mL. AcOH, 30 mL. ether, 0.2 mL. H2O, and 5 g. Zn, gives 2 g. V, light brown, b0.3 215-19° (bath), and some BzH; on one occasion, there results a small quantity of a compound, C17H16O5, m. 147° (possibly the lactone of 2,5,6-HO2C(MeO)2C6H4C6H4(OMe)CH2OH-5,2 or 2,5,6-HOCH2(MeO)2C6H4C6H4(OMe)CO2H-5,2). Oxidation of V with KMnO4 in H2O

gives VI; V, warmed with 25% NaOH at 100°, gives a black tar; V is unchanged by cold alkali and does not react with CH2(CO2H)2 and C5H5N (24 h. on the steam bath). Thebaine (5 g.) in 100 mL. boiling C6H6, treated (1 h.) with 5 g. MgI2 in 40 mL. C6H6 and 10 mL. ether and boiled 4 h., gives the MgI product (XIV); it degenerates rapidly on exposure to moist air; boiling 3 min. with 15% HCl, XIV gives a gum which with Me2SO4 and alkali does not give an identifiable compound XIV is not oxidized to a known **acid.** XIV and excess PhMgBr in C6H6, shaken 24 h. at room temperature, yield (+)-I.HClO4. Reduction of XIV in liquid NH3 with Na gives a compound (C19H24O3N2)2.HgI4. Definite compds. were not isolated from the reduction of XIV with LiAlH4. 3,4,6-Trimethoxyphenanthrene (12 g.) in 30 mL. AcOH at -5°, treated (1.5 h.) with 12.5 g. CrO3 in 3 mL. H2O and 18 mL. AcOH (temperature not above 30°), gives 4.5 g. 3,6-dimethoxy-1,4-phenanthraquinone (XV), orange, m. 223°, deep blue solution in concentrated H2SO4. XV and o-C6H4(NH2)2 in AcOH, heated 1 h. on the steam bath, give 3-hydroxy-7'-methoxynaphtho(1',2',1,2)phenazine, orange, m. 295-7°. XV (4 g.) in 75 mL. AcOH, treated with 4 mL. 30% H2O2 and heated 19 h. on the steam bath (3 mL. H2O2 added each 3 h.), give 0.5 g. 8-carboxy-7-(2-carboxyvinyl)-2-methoxy-1,4-naphthoquinone, bright yellow, with 0.5 mol. H2O, m. 273-5° (decomposition); the major portion of the oxidation product, on further oxidation with alkaline KMnO4, gives 1,2,3,4-C6H2(CO2H)4. Oxidation of 1.5 g. thebaol with 1.9 g. CrO3 in 0.5 mL. H2O and 12 mL. AcOH gives 0.4 g. XV.

L26 ANSWER 15 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1950:49353 CAPLUS
DOCUMENT NUMBER: 44:49353
ORIGINAL REFERENCE NO.: 44:9453f-i,9454a-g
TITLE: β- **Dihydrothebaine**
AUTHOR(S): Schmid, H.; Karrer, P.
CORPORATE SOURCE: Univ. Zurich, Switz.
SOURCE: Helvetica Chimica Acta (1950), 33, 863-73
CODEN: HCACAV; ISSN: 0018-019X
DOCUMENT TYPE: Journal
LANGUAGE: German
IT **115-37-7**, Thebaine
(reactions of)
RN 115-37-7 CAPLUS
CN Morphinan, 6,7,8,14-tetradehydro-4,5-epoxy-3,6-dimethoxy-17-methyl-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI For diagram(s), see printed CA Issue.
AB Thebaine with LiAlH4 gave 30% **dihydrothebaine** (I) (Ia, R = H),

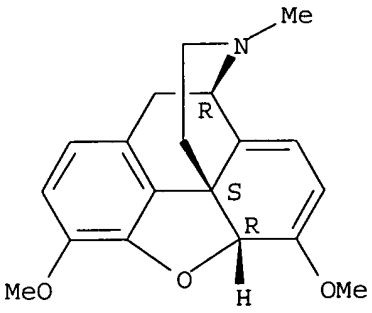
C19H23O3N, m. 171-2°, [α]D 307° (alc.), which was assigned the β-configuration. It shows an active H (Zerewitinoff) because of the weakly acidic phenolic hydroxyl and can be extracted from Et2O with 40% KOH solution to give a K salt. I gives an intense blue color with dichloroquinonechloroimine, a green color with FeCl3, and reduces NH3-AgNO3 solution Because of their unstability no definite acyl derivs. could be obtained. I was characterized as the picrate and as the methiodide, which crystallizes with 1 mol. C5H5N. The accompanying structure Ia is proposed because, like phenyl- (II) (Ia, R = Ph) and methyldihydrothebaine, it has an UV absorption maximum at 283 mμ, is very sensitive to **acids**, and is easily reduced. The phenolic **dihydrothebaine** (**prepared** by reduction of thebaine with Na and EtOH) and thebainone enol Me ether (**prepared** by heating codeine Me ether with NaOMe) are known and are distinguishable from I by their optical activity (25.5° and 9.6°, as against 307°).

In comparing the mechanism of the reaction between LiAlH4 and PhMgBr on thebaine, an intermediate cation B is postulated which, in the case of LiAlH4, stabilizes itself by attaching H-, forming I. Steric hindrance prevents a similar result with the Ph group of PhMgBr and the cation must rearrange as follows: the N-methylethylamine side chain splits cationically, and the resulting C13 electron pair reacts with C14 sym to form a double bond, forming an aromatic nucleus, simultaneously with the heterolysis of the C14C9 bond, whereby C14 becomes anionic and C9 cationic. By the reaction of C14- with C15 sym the result is the C14C15 bond. This intermediate cation C is then stabilized by the addition of Ph.sym. with the formation of a metalloorg. complex whose hydrolysis gives II. Thebaine (3 g.) in 48 cc. dry C6H6 was distilled to 20 cc. volume, diluted with 60 cc. absolute Et2O, treated with 500 mg. LiAlH4, refluxed 48 h. under a N or H atmospheric, the excess LiAlH4 destroyed with AcOEt, the mixture poured into ice water, **made** alkaline with NH4OH, filtered through Hyflo supercel, the residue rubbed with Na2CO3 and extracted thoroughly with Et2O-CHCl3, and the combined exts. washed with 2% KOH containing some NaHSO3, then with saturated NaCl solution, dried over Na2CO3, and concentrated to dryness to give I; picrate, m. 173° (decomposition); methiodide, gradually decompose above 120°, [α]D16 54° (c 0.931, absolute alc.). An Ac derivative could not be isolated, while BzCOCl yielded a resinous product. Warming with PhNHNH2 in AcOH also yielded a resin. It did not react with PhNCS in 14 days at 30°. I (30 mg.) in 10 cc. 0.1 N HCl showed [α]D13.5 >300°, dropping rapidly to a constant value of [α]D13.5 46.7° in 85 min. In AcOH the rotation dropped from 313° to 12.8° in 19 h. I (353 mg.) allowed to stand in 8 cc. water containing 310 mg. KHSO4 15 h. at 18°, diluted with water, and the **base** precipitated by dropwise addition of Na2CO3 solution, extracted with Et2O, worked up in the usual way, then chromatographed over Al2O3, yielded β-thebainone, m. 97-9° (AcOEt-Et2O-water), [α]D27 114.9° (c 0.496, alc.). I (630 mg.) in 6 cc. absolute EtOH hydrogenated in the presence of 400 mg. PtO2 pre-reduced in 15 cc. EtOH, filtered after 2 mols. H was absorbed, concentrated to dryness, and the residue taken up in water, **made** alkaline with NH4OH, extracted with Et2O, the Et2O extract washed with N KOH, then worked up in the usual way, and chromatographed over Al2O3 with C6H6-Et2O 10:2, gave tetrahydro-β-**dihydrothebaine**, m. 143.5-4.5° (Et2O-petr. ether, Et2O-alc.-water), [α]D20 -17.5° (c 0.986, absolute alc.); acetate, m. 110-11°. It gives an intense blue-violet color with Gibbs reagent, a brown precipitate with FeCl3 solution, changing to a green solution, and the potentiometric titration of the acetate-HCl in 0.1 N KCl solution at a

concentration of 9.03 + 10-4 shows pK = 9.31, indicating that the acetate is an O-Ac compound

L26 ANSWER 16 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1939:23505 CAPLUS
DOCUMENT NUMBER: 33:23505
ORIGINAL REFERENCE NO.: 33:3383d-i,3384a-i,3385a-b
TITLE: Reduction studies in the morphine series. VII. Thebaine
AUTHOR(S): Small, Lyndon; Browning, Geo. L., Jr.
SOURCE: Journal of Organic Chemistry (1939), 3, 618-37
CODEN: JOCEAH; ISSN: 0022-3263
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
IT **115-37-7**, Thebaine
(and derivs.)
RN 115-37-7 CAPLUS
CN Morphinan, 6,7,8,14-tetradehydro-4,5-epoxy-3,6-dimethoxy-17-methyl-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



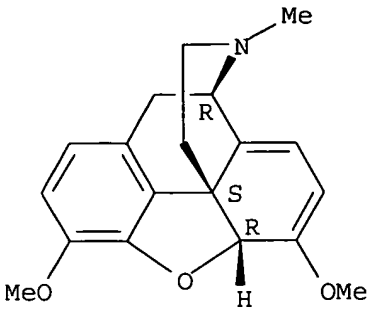
GI For diagram(s), see printed CA Issue.
AB cf. C. A. 29, 1829.2. Codeine Me ether (I) can be caused to rearrange to a phenolic isomer, thebainone Me enolate (II). I, m. 142°, [α]D22 -194.5, (10 g.) in 80 cc. absolute alc. NaOEt (containing 2.4 g. Na) was heated at 100° for 4 hrs. in a sealed tube. The contents were diluted with 150 cc. H2O and the alc. was removed at 25° under vacuum in the presence of H2. The product was salted out with NH4Cl, yielding 9.5 g. of crystalline II, C19H23NO3, m. 154-6°, [α]D22 9.6° (alc., c 0.57), readily hydrolyzed and somewhat unstable on long standing. Addition of excess KI to 0.5 g. II in 3 cc. of warm 3 N HCl gave the thebainone HI salt, m. 257-60° (decomposition), yielding thebainone, m. 145-7°, [α]D24 -46.6°; oxime, m. 285-7°. The ease of opening of the ether ring of I is ascribed to the position of the H atom on C-6 which appears to lie in a configuration with respect to the cyclic ether O atom that favors the change and which may be activated by the 7,8-double linkage. Reduction of 4 g. II in 300 cc. alc. under reflux in an atmospheric of H2 by the addition of 20 g. Na with stirring, addition of 300 cc. of O-free H2O, removal of the alc. under a vacuum in the presence of H2, and treatment with excess CO2 gave a nearly white crystalline product, purified by extraction with Et2O, yielding 2.1 g. of Δ-5,6-dihydrothebainone methyl enolate (III), m. 164.0-5.5°, [α]D25 -115.7° (alc., c 1.02), converted by **acid** to dihydrothebainone. Reduction of 4 g. II with 0.1 g. PtO2 in absolute alc. with 1 mol. H2 gave 2.4

g. III. The fumarate of III in aqueous solution hydrolyzes to dihydrothebainone fumarate and the sp. rotation drops from -64.4° to -39.0° in 60 min. The structure advanced for III is based on the exclusive reduction of II at the 7,8-unsatn. and has been already assigned to an oily product (cf. Wieland and Kotake, C. A. 19, 2827) obtained from the hydrogenation of thebaine (IV) under neutral conditions. This hydrogenation has been reinvestigated. A suspension of 25 g. IV in 150 cc. of 95% alc. was shaken under H2 with 2 g. of Pd-BaSO4 (5% Pd) and 0.5 g. NaHCO3 until 2.2 mols. of H2 were adsorbed. From the filtered solution III crystallized out immediately in 47% yield (11.8 g.). The alc. mother liquors were boiled and treated with fumaric **acid**, forming 18% of dihydrothebainol fumarate 6-Me ether (V). The mother liquor was evaporated to a thick oil, taken up in H2O, neutralized with NH4OH and extracted with Et2O, giving a yellow oil which was dissolved in 50 cc. of hot alc. and treated with 6.3 g. picric **acid**, yielding 13.4 g. of crystalline tetrahydrothebaine picrate equivalent to 7.7 g. of tetrahydrothebaine, m. 81-3°. The total yield of identified products was 24.1 g. or 96% of the starting material. Purification from absolute alc. gave V, m. 198-201° (decomposition), [α]D22 -28.1° (H2O, c 0.85), converted to the free **base**, recrystg. from boiling iso-Pr2O (peroxide-free) and benzene and subliming in a high vacuum at 120° to yield silky white needles of dihydrothebainol 6-Me ether, C19H27NO3, m. 140.5-2.0°, [α]D21 -23.4° (alc., c 1.024). The reduction mechanism is discussed. Reduction of theba.acte.ine with Na results in reductive scission of the ether ring, yielding a phenolic **dihydrothebaine** (VI), an isomer of II. IV (30 g.) in 400 cc. alc. was refluxed under H2 with stirring, and 105 g. Na and 1200 cc. alc. were added in 2 hrs. The product was treated with 50 cc. H2O, diluted with alc. and saturated with CO2. The neutralized mixture was press-filtered through canvas and the filtrate was concentrated under a vacuum to a thick oil which solidified under H2O overnight. Crystallization from AcOMe gave 15 g. of quadrangular prisms of VI, C19H23NO3, m. 152-4°, [α]D27 25.5° (alc., c 1.096) (cf. Freund and Holthof, Ber. 32, 175(1899)). Catalytic reduction of VI gave quant. yields of Δ-6,7-dihydrothebainone Me enolate (VII), C19H25NO3, m. 127-8°, [α]D27 -8.0° (alc., c 0.503), converted by treatment with N HCl for 5 mins. and precipitation with Na2CO3 to dihydrothebainone; oxime, m. 240-2° (decomposition). The isomerism of VII and III is due only to a difference in location of the enolic double bond. Hydrolysis of 20 g. VI with dilute KHSO4 at 25° for 5 hrs. gave about 1 g. of thebainone, a small amount of α-thebainone, m. 184-5°, [α]D27 158.5° (CHCl3, c 0.511), and 15.4 g. β-thebainone (VIII), C18H21NO3, m. 98-9°, [α]D27 114.9° (alc., c 0.496), purified through the H ClO4 salt, m. 149-57°, [α]D27 67.3° (MeOH, c 0.505), or the HBr salt, m. 168-9° (decomposition), [α]D27 61.1° (H2O, c 0.516); HI salt, m. 150-5° (decomposition), [α]D27 55.3° (H2O, c 0.452); picrate, m. 172-83° (decomposition), [α]D27 43.8° (Me2CO, c 0.502); oxime fumarate, m. 220.5°, [α]D27 46.0° (H2O, c 0.370); semicarbazone picrate, m. 203-4°. VIII appears to differ from the previously known types of morphine derivs. in the configuration of the asym. C atom 14. VIII can be converted successively to the following derivs., all of which are isomeric with the corresponding compds. derived from the previously known thebainone: β-dihydrothebainone (IX); β-dihydrothebainonemethine (X); β-dihydrothebainonedihydromethine (XI); and β-thebenone (XII). VIII-HClO4 (10 g.) in 250 cc. alc. was catalytically reduced with 1 mol. H2 in the presence of 50 mg. PtO2 to give the β-dihydrothebainone-

HClO4, m. 254-5°, [α]D24 -32.5° (H2O, c 0.400), which was neutralized by NH4OH and extracted with Et2O to yield IX, C18H23NO3, [α]D27 -48.1° (alc., c 0.499); HCl salt, m. 245-8°, [α]D27 -34.4° (H2O, c 0.494); HBr salt, m. 225.5-7.5°, [α]D27 -31.5° (H2O, c 0.508); picrate, m. 202-15° (decomposition), [α]D27 -16.5° (Me2CO, c 0.121); MeI derivative (XIII), m. 149-54°; oxime, m. 225-6°, [α]D21 -100.4° (alc., c 0.438). XIII (6 g.) was boiled with 40% NaOH for 20 mins. The resulting Na salt was triturated with H2O and the suspension was extracted with Et2O, yielding 3.6 g. of needles of X, C19H25NO3, m. 183-4°, [α]D28 -257.9° (alc., c 0.473); HClO4 salt, m. 225.5-6.0°; picrate, m. 164-5°, [α]D27 -181.1° (Me2CO, c 0.475); oxime, m. 160-2°. Catalytic reduction of 2 g. X in dilute AcOH with 10 mg. PtO2 and 1 mol. H2 in 15 mins., neutralization with Na2CO3 in the presence of Et2O, and crystallization from alc. or Me2CO gave XI, C19H27NO3, m. 177-8°, [α]D27 63.8° (CHCl3, c 0.502); HBr salt, m. 260.0-0.5°, [α]D28 24.0° (H2O, c 0.500); HClO4 salt, m. 232.5-3.5°, [α]D28 23.8° (MeOH, c 0.505); picrate, m. 203-7°, [α]D27 18.2° (Me2CO, c 0.495). XI (0.6 g.) in hot benzene was treated with 0.2 cc. MeI and the resulting white powder (0.85 g.) was boiled with 40% NaOH, diluted with H2O, extracted with Et2O and recrystd. from alc., yielding 0.5 g. of rods of XII, C17H20O3, m. 189-90°, [α]D28 113.6° (alc., c 0.559); oxime, m. 176-7°, [α]D28 30.6° (alc., c 0.506). This is the 1st well established example of isomerism at the C-14 atom in the morphine series.

L26 ANSWER 17 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1932:3858 CAPLUS
DOCUMENT NUMBER: 26:3858
ORIGINAL REFERENCE NO.: 26:474g-i,475a
TITLE: **Acid** rearrangement of morphine alkaloids. II. **Preparation** of the true thebainone and the action of concentrated hydrochloric **acid** upon thebaine
AUTHOR(S): Schopf, Clemens; Hirsch, Hans
SOURCE: Ann. (1931), 489, 224-51
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
IT **115-37-7**, Thebaine
(reaction with concentrated HCl)
RN 115-37-7 CAPLUS
CN Morphinan, 6,7,8,14-tetradehydro-4,5-epoxy-3,6-dimethoxy-17-methyl-, (5α)- (9CI) (CA INDEX NAME)

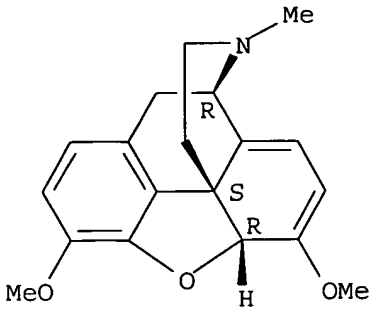
Absolute stereochemistry.



AB cf. C. A. 22, 430. Thebaine (I) (10 g.), gradually added to 58 g. SnCl2.2H2O in 120 cc. 37.2% HCl and heated in a pressure flask to 70° during 15 min. and held at that temperature for 15 min., cooled, 12 parts H2O added, the **base** liberated with alkali and extracted with CHCl3, gives 19% of metathebainone (II), and about 30% of thebainone (III); details are given for the **preparation** of III from the red solution of I in concentrated HCl with SnCl2 (12% yield) and also from **codeinone** (IV) with HCl and SnCl2 (44% yield). If 3 g. IV in 36 cc. concentrated HCl is treated with 17.4 g. SnCl2 and reduced as above, there results 25% of III, 3% of II and 49% of codeine. In another experiment a small quantity of a compound, m. 155-8°, yielding an oxime, (C18H21O3N2)2(?), does not m. 300°. III, m. 151-2°, crystals with 0.5 mol. H2O, lost at 100° in vacuo, soluble in alkali with a citron-yellow color; HI salt, m. 258-9°; methiodide (V), m. 223°: oxime, m. 180-3°, crystals with 0.5 mol. H2O (HCl salt, m. 290-1°). Catalytic reduction of III gives the dihydro, derivative, m. 245°; V, Ac2O and AcONa, heated 1 hr., and the I removed with AgOAc, give 3,4,6-triacetoxyphenanthrene, m. 165-7°, which also results from acetylthebaol and HBr, followed by acetylation. The red solution of I in concentrated HCl, treated with 2 N NAOH until the ppt which appears goes into solution and extracted with Et2O, gives **codeinone** (0.7 g. from 10 g. I); in an attempt to isolate the oxime from the red solution, an addition compound, C18H22O4N2, crystallizing with 1 mol. H2O, m. 142-4° and then 210-2°. **Codeinone** (0.25 g.) in 3 cc. concentrated HCl is recovered unchanged after 0.5 hr. at room temperature (80% yield). I.HCl (5 g.) and 5.5 g. SnCl2 in AcOH, heated 1 hr. at 150-60°, give 2.6 g. of methebenine- HCl, m. 244-5°.

L26 ANSWER 18 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1917:9426 CAPLUS
DOCUMENT NUMBER: 11:9426
ORIGINAL REFERENCE NO.: 11:1954f-i,1955a-i,1956a-d
TITLE: Thebaine. V. Reduction of thebaine and phenyldihydrothebaine
AUTHOR(S): Freund, Martin; Speyer, Edmund
CORPORATE SOURCE: Univ. Frankfurt a/M
SOURCE: Ber. (1916), 49, 1287-307
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
IT **115-37-7**, Thebaine
(reduction of)
RN 115-37-7 CAPLUS
CN Morphinan, 6,7,8,14-tetradehydro-4,5-epoxy-3,6-dimethoxy-17-methyl-, (5α)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



GI For diagram(s), see printed CA Issue.

AB cf. Ibid 39, 844(1906). In the Knorr formulas for morphine, codeine and thebaine (a) there are 2 aliphatie double bonds and F. has for some time been trying to obtain exptl. evidence for the presence or absence of these C:C bonds. The choice of reducing agents for (a) is limited to those which can be used in alkaline solution, for (a) easily undergoes deep-seated changes in **acid** solution When (a) in boiling alc. is treated with excess of Na, it does, in fact, take up 2 H atoms; these, however, do not add at a C:C bond but merely open the O bridge (Ber. 38, 3242 (1905)), and the resulting **dihydrothebaine** (b) should, if K.'s formula is correct, still contain the 2 aliphatic C:C bonds; it is therefore quite surprizing that it does not take up more H in spite of the great excess of nascent H in the energetic reaction. F. then tried another derivative of (a) differing from (b) only in having a Ph group substituted for 1 of the H atoms of the C6H6 nucleus, viz. phenyldihydrothebaine (c) (Ber. 38, 3248(1905)), but which, unlike (b), is unusually stable not only towards alkalies but towards **acids** also and it was to be expected, if it contains aliphatic C:C bonds, that their presence could be detected by some of the numerous **acid**-reducing agents. Such, however, is not the case; the usual reducing agents, even the powerful Tafel **method** of reducing electrolytically in H2SO4 at a **prepared** Pb cathode, do not attack (c). In the presence of colloidal Pd, (c) does take up 2 atoms of H, giving almost quant. a compound, phenyltetrahydrothebaimine (d), which, however, is a secondary **base**, so that here again the H has not been added at a C:C bond. The behavior of (c) towards halogens also does not harmonize with the view that it contains C:C bonds di-Cl and di-Br derivs. are obtained but in poor yields. v. Braun's test for C:C bonds (C. A. 9, 321) also was negative with (c); treatment of its Ac derivative with BrCN gave a Br-free compound having no basic properties and containing 5.96% N, apparently formed by the addition of CN and the splitting off of Me as MeBr. In view of these facts, F. believes that (c), and therefore (a) also, contains no aliphatic C:C bonds and suggests for the latter the formula (I) and analogous formulas for morphine and codeine; he shows, by means of profuse graphical formulas, how the various reactions of these alkaloids can be explained on the basis of his formula. To (d) he assigns the structure (II). (d) is **prepared** by shaking 15 g. (c) in 100 cc. H2O and 40 cc. of 10 %AcOH with 100 cc. of Pd colloid solution (0.5 g. Pd) in H 4 hrs., filtering, making alkaline with NH4OH and warming until the (d) becomes crystalline; it crysts. from alc. in leaflets, m. 122°, [α]D 27.6° in dilute AcOH, soluble in alkalies, repptd. by NH4Cl, instantly decolorizes KMnO4 in H2SO4; its salts with HCl, HClO4, HBr and HI are oily. Nitroso derivative, obtained in small amount from 2 g. (d) in 30 cc.

of 10% AcOH and 10 cc. of N NaNO2, red warty crystals from alc., decomps. 193°, soluble in alkalies, repptd. by NH4Cl. Bis[phenyltetrahydrothebaimine]urea, CO(NMeC24H25O3)2, from 0.5 g. (d) in 5 cc. C6H6 boiled gently for 5 min. with 5 cc. of 10% COCl2 in CHCl3, felted needles from 96% alc., m. 138-9°, insol. in H2O and HCl. Phenyltetrahydrothebaiminemethin methiodide, C24H25O8NMe8I, obtained in 5.5 g. yield, together with 7.5 g. (d).HI, from 10 g. (d) in C6H6 allowed to stand 6 hrs. with 5 cc. MeI, serrated columns from alc., m. 233-5°; when boiled with dilute NaOEt it decomps. into NMe3, HI and phenyltetrahydrothebenol (e), C24H24O3, columns from glacial AcOH containing a few drops of H2O, m. 86°. When (d) is heated 5 min. at 140° with 3 parts p-MeC6H4SO3Me it forms the compound, C24H25O3NMe3O3SC6H4Me, needles from 96% alc., m. 245°, soluble in NaOH, repptd. by small amts. of NH4Cl and redissolved by an excess, easily soluble in HCl and hot H2O, decomposed by boiling aqueous alc. NaOH into NMe3 and (e). When 10 g. (c) in 50 cc. boiling HCl (d. 1.1) is treated with 5 cc. of 30% H2O2 the odor of BzH soon develops and a red-yellow oil seps.; the excess of H2O2 is destroyed by adding SO2 until a clear solution results on heating, then KI is added to the hot solution until there is no further separation of oil; this on crystallization from 96% alc. yields 5 g. of 6-sided leaflets, sinter 185°, m. 203° (foaming), of the hydriodide, C25H27O3NCl2.HI.H2O, of dichlorophenyldihydrothebaine, warty crystals from alc., sinters 130°, m. 135-40°, precipitated from its NaOH solution by NH4Cl. Methiodide, obtained quant. from the components under pressure at 100°, rodlets from AcOH, m. 230°; when digested with NaOEt until dissolved, diluted with 2 vols. H2O and treated with NH4Cl, it gives a non-crystallizable **base** which in alc. with HCl and KI yields des-N-methyldichlorophenyldihydrothebaine hydriodide, C26H29O3NCl2.HI, felted needles from alc., sinters 180°, m. 205°; methiodide, from the **base** and MeI under pressure at 100°, very soluble in alc. and not isolated, converted by boiling NaOEt into NMe3 and dichlorophenyldihydrothebenol, needles from alc., m. 160-2°. From 15 g. (c) in 100 cc. cold AcOH treated within the course of 10 min. with 50 cc. of a Br solution (24 cc. Br in 100 cc. glacial AcOH), then with 40 cc. of HBr (d. 1.7), boiled and allowed to stand, is obtained a light yellow perbromide, octahedrons from AcOH, decomps. 195-6°; this, digested warm with SO2 and a little alc. until dissolved, yields dibromophenyldihydrothebaine hydrobromide, leaflets from 50% alc., sinters 180°, m. 198° (foaming) (yield, 7.5 g.). The mother liquors from the perbromide, decolorized with SO2 and diluted with 3 vols. H2O, deposit a tarry mass which in alc. with NH4OH yields an amorphous **base**, needles or rodlets from alc., m. 190°, contains Br, insol. in aqueous but soluble in alc. NaOH, repptd. by NH4Cl, reduced in alc. by Na to (c).HI. Dibromophenyldihydrothebaine, from the HI salt in dilute alc. with NH4OH, needles from alc., m. 165-8°, gives with KI and HCl the hydriodide, tables from alc., m. 205-8° (foaming). When 3 g. of the HBr salt in alc. are treated with 20% H2SO4 and reduced 2 hrs. with a 12 amp. current at a **prepared** Pb electrode, it forms phenyltetrahydrothebaine, C25H29O3N, isolated as the hydrobromide, leaflets from dilute alc., decomps. 175-6°; yield, almost quant. Methiodide, columns, with 1 mol. H2O, m. 215°. Boiled 15 min. with HI, the **base** gives norphenyltetrahydrothebaine hydriodide, C23H25O3N.HI, felted needles from H2O, decomps. 195°. When 1 g. acetylphenyldihydrothebaine in 5 cc. CHCl3 is boiled 1 min. with 1 g. BrCN in 5 cc. CHCl3 there is obtained 1 g. of a compound C27H26O4N2, does not crystalline, m. around 90°, has no basic properties. From 10 g. (c) in

250 cc. H2O and 40 cc. KOH (1:1) treated boiling in the course of 0.5 hr. with 40 cc. of 30% H2O2 is obtained a small amount of an **acid**, phenyldihydrothebainic **acid**, C24H25O5N, precipitated by HCl from alc. NH4OH in serrated columns, decomps. 243-5°, contains only 1 MeO group, soluble in concentrated **acids** with intense yellow color, unattacked by SO2. Barium salt, C24H23O5NBa, needles, decomps. 280°. Magnesium salt, crystalline Silver salt, amorphous.

=> log y

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